Prevention and Treatment of HIV/AIDS Among Drug Using Populations:

A Global Perspective

Table of Contents

Executive Summary

On January 11–12, 2010, the National Institute on Drug Abuse (NIDA) and the International AIDS Society (IAS) held a consultation meeting, "Prevention and Treatment of HIV/AIDS among Drug Using Populations: A Global Perspective," in Washington, D.C. The overarching goal of the meeting was to advance understanding of the global HIV and substance abuse epidemics and highlight the importance of including drug abusers—particularly injection drug users (IDUs)—in any comprehensive, multidisciplinary approach to HIV prevention and treatment. It also was intended to spur progress on the development of comprehensive, integrated approaches that combine addiction treatment with prevention and treatment of HIV and co-infections.

Speakers were chosen for their broad knowledge in areas such as HIV and substance abuse treatment and prevention and their engagement in international research. In addition, a panel was held with representatives from organizations charged with addressing HIV and substance abuse policy. Breakout sessions related to each presentation were held. Participants were asked to develop recommendations for HIV prevention and treatment of substance abusers based on existing scientific evidence and to identify priority areas for further research. Breakout session recommendations are found in Appendix A.

The meeting reflected a growing recognition and consensus, not only by the scientific community but also by policymakers, of the importance of comprehensive prevention for drug-using populations, especially IDUs. Elements of comprehensive HIV prevention include: community-based outreach, substance abuse treatment (including opioid substitution therapy and other medication-assisted therapies as well as behavioral interventions), needle and syringe exchange programs, HIV testing, and linkage to care for HIV and comorbid conditions. Participants called for implementation of science-based approaches to HIV and drug abuse prevention and treatment and advocated for the removal of barriers to implementation. They also recognized the need for implementation science research to study the rollout of these interventions in diverse settings.

Overview of the Report

Chapter 1, "Introduction," describes an urgent need to address the global substance use epidemic in order to reduce new HIV infections. The meeting provided an opportunity for international experts in the fields of HIV and substance abuse to develop science-based research and clinical recommendations for prevention and treatment of HIV/AIDS among drug-using populations. A major focus of the meeting was the application of the "seek, test, treat, and retain" paradigm of expanded antiretroviral therapy (ART) to drug-using populations. This paradigm uses aggressive outreach to high-risk, hard-to-reach populations, HIV testing, linkages to HIV treatment and other services, and retention of individuals in care to enhance the health of drug users and stem the spread of HIV in the general population. The meeting provided a forum for the presentation of data countering the erroneous assumption that addictive disorders make HIV-positive patients virtually untreatable with modern antiretroviral therapy. The chapter also describes the factors that led NIDA and IAS to hold the January 2010 meeting and provides a description of the meeting's process and outcomes.

Chapter 2, "Global Strategy for HIV and Drug Use," summarizes presentations on current activities and policies from a panel that included the President's Emergency Plan for AIDS Relief (PEPFAR), the Office of National AIDS Policy (ONAP), the Office of National Drug Control Policy (ONDCP), the Centers for Disease Control and Prevention (CDC), the NIH Office of AIDS Research (OAR), the National Institute of Allergy and Infectious Diseases (NIAID), and the United Nations Joint Programme on HIV/AIDS. The presentations made clear that the United States has adopted new directions in its policy on drugs and HIV/AIDS. This has significant ramifications, not only for domestic strategy but also because it will significantly affect the global dual epidemic of drug use and HIV/AIDS, particularly injection drug use. The panel supported expanded access to HAART for drug users using the "seek, test, treat, and retain" paradigm. Panel members agreed that evidence-based substance abuse treatment and prevention are essential to a comprehensive HIV prevention strategy. The panel endorsed

proven harm-reduction measures, such as needle and syringe exchange programs (NSPs), sexually transmitted disease treatment and vaccines, condom distribution, and educational information adapted to local cultural and social contexts. The need for implementation science to help bridge the gap between scientific knowledge and effective program implementation also was strongly supported.

Chapter 3, "Comprehensive Approaches to HIV Prevention for People Who Use Drugs," describes how substance use and abuse has been shown to be associated with an increased risk of HIV infection in key populations worldwide and highlights the importance of including drug abusers—particularly injection drug users—in comprehensive strategies for HIV prevention and treatment. It describes the challenges and barriers to treating HIV in drug-using populations and suggests strategies to overcome them. The chapter describes the complementary interventions: community-based outreach, needle and syringe exchange, substance abuse treatment, HIV testing and linkage to care, and integration of services that have been proven most useful in comprehensive HIV/AIDS prevention for drug users. A key theme of this chapter is that substance abuse treatment is HIV prevention. Drug users who enter and continue in treatment are more likely than those who remain out of treatment to reduce risky activities, such as sharing needles and injection equipment or engaging in unprotected sex, and are more likely to initiate highly active antiretroviral therapy (HAART) and remain in treatment. The chapter describes current substance abuse treatments for specific types of drugs, addresses the most prevalent co-infections found in this population—i.e., hepatitis C and tuberculosis—and describes drug–drug interactions.

Chapter 4, "Expanded HAART to Improve Individual and Public Health Outcomes," describes dramatic reductions in morbidity and mortality in HIV-infected patients associated with the rollout of HAART in resource-rich and resource-limited regions of the globe. It presents the new paradigm, "Seek, Test, Treat, and Retain," of expanding HAART coverage as a tool in HIV prevention. The components of this paradigm include outreach to high-risk, hard-to-reach populations; HIV testing; linkages to HIV treatment and other services; and maintaining individuals in care. A driving force behind this strategy is the proven, patient-centered benefits of HAART in decreasing AIDS-related morbidity and mortality and recent findings on the direct and multiple secondary benefits of the expansion of HAART coverage. Data are presented showing that aggressive expansion of HAART in injection drug users can lead to reductions in community viral load and decreases in new infections. Expansion of HAART has not been shown to lead to increased antiviral drug resistance. Yet HIV testing is not the norm at substance abuse treatment centers. This chapter also addresses basic clinical questions concerning when to start ART, which regimen to use, and when to change regimens, and it presents research and guidelines offering advice on these issues. It also examines the challenges of adherence to ART among drug-using populations.

Chapter 5, "Drug Abuse, HIV/AIDS, and the Criminal Justice System: Challenges and Opportunities," describes the dichotomy between the public health and criminal justice perspectives with regard to substance abuse. It describes how the "War on Drugs" resulted in increased incarceration rates for drug users and increases in HIV, TB, and HCV infections. Despite an international framework that calls for provision of the same or equivalent prevention, care, treatment, and support for HIV/AIDS that is available to people in the community outside of prison, few prison systems offer this. Missed opportunities for treatment of HIV and substance abuse as well as TB and HCV are described. The opportunities for "seek, test, treat, and retain" in criminal justice settings are explored, including the importance of linkages to care upon community reentry. Participants endorsed the need for more research on implementation of "seek, test, treat, and retain" in criminal justice settings.

Chapter 6, "Human Rights and At-Risk and Vulnerable Populations," describes human rights in the context of HIV and substance abuse prevention and treatment and addresses the problems of stigma and discrimination. In some cases, discrimination against people living with, or at high risk for, HIV is institutionalized in national and local laws. Fear of stigma and discrimination makes people less likely to seek care and treatment, adhere to treatment, or disclose their HIV status to their sexual partners. The chapter focuses on several populations that tend to have a higher prevalence of HIV infection than the general population: women in the developing world, sex workers, and men who have sex with men. Effective interventions for each of these populations are described.

Chapter 1. Introduction

On January 11–12, 2010, the National Institute on Drug Abuse (NIDA) and the International AIDS Society (IAS) held a consultation meeting in Washington, D.C. The overarching goal of the meeting was to advance understanding of the global HIV and substance abuse epidemics and highlight the importance of including drug abusers, particularly injection drug users (IDUs), in any comprehensive, multidisciplinary approach to HIV prevention and treatment. Titled "Prevention and Treatment of HIV/AIDS Among Drug Using Populations: A Global Perspective," the meeting provided an opportunity for international experts in the fields of HIV and substance abuse to develop science-based research and clinical recommendations for prevention and treatment of HIV/AIDS among drug-using populations. A major focus of the meeting was the application of the "seek, test, treat, and retain" paradigm of antiretroviral therapy (ART) to drug-using populations as a means of enhancing the health and well-being of drug users and as a crucial element in stemming the spread of HIV in the general population. The meeting provided a forum for the presentation of data countering the erroneous assumption that addictive disorders make HIV-positive patients virtually untreatable with modern antiretroviral approaches because of lack of medication compliance and uncooperative behaviors. It also was intended to spur progress on the development of comprehensive, integrated approaches that combine addiction treatment with prevention and treatment of HIV and co-infections.

The International AIDS Society is the world's leading independent association of HIV professionals. IAS convenes the world's foremost international conferences on HIV and AIDS and specialized meetings, providing critical platforms for presenting new research, promoting dialogue, and building consensus to advance the global fight against HIV.

The National Institute on Drug Abuse is the U.S. Federal focal point for research on drug abuse and addiction. It is part of the National Institutes of Health, U.S. Department of Health and Human Services. NIDA's mission is to lead the nation in bringing the power of science to bear on drug abuse and addiction.

A Timely Opportunity: Why This Meeting Was Held

There is an urgent need for global policy guidance, research, and programming that addresses the associations between HIV and various types of substance abuse. NIDA and IAS recognized that the time was right for a meeting of experts who could present a global perspective on these issues and lay the groundwork for future directions in HIV prevention and treatment in drug-using populations. This urgent need is reinforced by the following facts:

1. Injection drug use accounts for 30% of people living with HIV outside sub-Saharan Africa, and the twin IDU and HIV epidemic also is emerging within Africa, adding a significant burden to already high rates of infection. HIV treatment for IDUs and other drug abusers is complicated by the need to manage drug dependence and its consequences, as well as the high incidence and prevalence of comorbidities, including hepatitis and tuberculosis (TB).

2. Studies show that many countries are experiencing an epidemic of the use of methamphetamine and other stimulant drugs by injection and noninjection routes. Many of these substances are associated with an increase in risky sexual behaviors.

3. A lack of access to effective substance abuse treatment, especially opioid substitution therapy, is a major factor in fueling HIV transmission and undermining the success of ART programs among drug-using populations. For example, in Eastern Europe and Central Asia, where drug use is the main driver of HIV, less than 1% of people who inject drugs have access to methadone or buprenorphine maintenance therapy. These treatments are illegal in Russia, which is home to 69% of people living with HIV in this region.

4. In many countries, punitive drug policies and harsh criminal justice strategies undermine HIV prevention

and treatment efforts for drug users, affecting access and retention in treatment, and preventing access to harm reduction services. Efforts to scale up prevention and treatment of HIV/AIDS through a comprehensive, multidisciplinary approach that includes drug users must address the policies and criminal justice interventions that hamper these efforts and address the treatment and prevention needs of those in criminal justice settings.

5. Drug-using populations have not received adequate attention from HIV/AIDS scientists and clinicians. They are frequently excluded from research, based on assumptions that drug users will not be compliant with protocols in clinical trials. In many countries, active substance abuse is among the criteria for exclusion from enrollment in ART.

Process and Outcomes

The agenda addressed issues that relate to drug-using populations worldwide in order to inform discussion, debate, and meeting outcomes. Speakers were chosen for the consultation meeting because of their broad knowledge in areas such as substance abuse treatment and HIV prevention and the "seek, test, treat and retain" model and its challenges for drug users. Most of the speakers are engaged in collaborative bilateral or multilateral research on HIV/AIDS and drug abuse with partners in regions highly affected by the twin epidemic. In addition, a panel was held with representatives from agencies and organizations charged with addressing HIV and substance abuse policy. Panelists presented the current plans of their organizations, which included the President's Emergency Plan for AIDS Relief (PEPFAR), the Office of National AIDS Policy (ONAP), the Office of National Drug Control Policy (ONDCP), the Centers for Disease Control and Prevention (CDC), the NIH Office of AIDS Research, the National Institute of Allergy and Infectious Diseases (NIAID), and The United Nations Joint Programme on HIV/AIDS. (The agenda is found in Appendix B.)

The co-chairs who facilitated the meeting are renowned researchers working on the cutting edge of HIV and drug abuse research. Dr. Julio Montaner is an international leader in HIV/AIDS research and the president of the International AIDS Society. He is a professor of Medicine at the University of British Columbia and is currently studying the impact of expanded HAART coverage among injection drug users. Dr. Charles O'Brien is Kenneth A. Appel Professor and Vice Chair of Psychiatry at the University of Pennsylvania and Chief of Psychiatry at the Philadelphia Veterans Administration Medical Center. He established and directs a clinical research program that has had a major impact on the treatment of addictive disorders.

The meeting was designed so that formal presentations and related questions for speakers took place during the first sessions of each day, followed by breakout sessions on related topics at the end of each day. During the breakouts, participants were asked to develop: (1) recommendations for enhancing HIV prevention and treatment of substance abusers based on existing scientific evidence; and (2) priority areas for further research. After these sessions, the resulting recommendations and priority areas for further research were presented to all meeting participants.

This report highlights the information presented over the course of the consultation meeting and presents the key recommendations for HIV prevention and treatment of substance abusers. Overall, the NIDA/IAS consultation meeting presented a unique opportunity to advance global understanding of the wide-reaching impacts of substance abuse on the HIV epidemic.

Chapter 2. Global Strategy for HIV and Drug Use

At the January 2010 consultation meeting, a panel was held with representatives from agencies and organizations charged with addressing HIV and substance abuse policy. U.S. panelists presented the current plans of their organizations, which included the President's Emergency Plan for AIDS Relief (PEPFAR), the Office of National AIDS Policy (ONAP), the Office of National Drug Control Policy (ONDCP), the Centers for Disease Control and Prevention (CDC), the NIH Office of AIDS Research, and the National Institute of Allergy and Infectious Diseases (NIAID). The United Nations Joint Programme on HIV/AIDS also was represented and presented on international initiatives relating to injection drug use. As illustrated by their statements, presented in this chapter, the United States has adopted new directions in drugs and HIV/AIDS policy. The administration's new position has significant ramifications, not only for domestic strategy, but also because it will significantly impact the global dual epidemic of drug use and HIV/AIDS, particularly injection drug use. Overall, the panel endorsed support for scaling up the following evidence-based strategies:

- Integrate, coordinate, and expand prevention interventions, including syringe and needle exchange programs (NSP), drug treatment, outreach, testing and counseling, linkage to HIV care for HIV-positive individuals, sexually transmitted disease (STD) treatment and vaccines, condom distribution, structural interventions, and educational information.
- Expand access to highly active antiretroviral therapy (HAART) for both injection and non-injection drug users using the Seek, Test, Treat, and Retain paradigm.
- Include substance abuse treatment and prevention as essential components of a comprehensive HIV prevention strategy.
- Strengthen the monitoring and evaluation of HIV prevention, treatment, and care delivery.

Furthermore, the panel expressed agreement that future research efforts should focus on:

- Expanding implementation/operational research to better inform program impact; improve service delivery; optimize outcomes; and adapt the program to local HIV epidemiologic, cultural, and social contexts;
- Addressing the problem of late diagnoses among injection drug users to optimize the potential beneficial effects of HAART in the early stages of the disease for this often-neglected population;
- Developing integrated delivery of services for the prevention and control of HIV and related co-infections and comorbidities;
- Developing strategies to improve adherence to treatment and reduce stigma among drug-using populations;
- Understanding the relationship between the stage of infection and the efficiency of transmission.

In light of these consensus statements, it is clear that the time is right to take action to optimize the beneficial effects of prevention, treatment, and care activities for drug-using populations across the globe. Efforts should focus on closing the coverage gap; expanding access and utilization; and scaling up tailored, comprehensive programs appropriate to local needs.

President's Emergency Plan for AIDS Relief

The President's Emergency Plan for AIDS Relief was launched in 2003 by President George W. Bush to combat AIDS. In the first 5 years of the program, PEPFAR focused on establishing and scaling up prevention, care, and treatment programs in low-resource settings. During its first phase, PEPFAR supported the provision of treatment to more than 2 million people; the provision of care to more than 10 million people, including more than 4 million orphans and vulnerable children; and treatment services for the prevention of mother-to-child (MTC) transmission during nearly 16 million pregnancies.

Now in its second phase, a new program strategy is underway at PEPFAR that supports the U.S. Government's overall emphasis on improving health outcomes, increasing program sustainability and integration, and strengthening health systems. During 2010 and beyond, PEPFAR will be working

closely with country teams to translate, prioritize, and implement this strategy in a manner appropriate to the country context. More information on the broader strategic framework for PEPFAR activities can be found at www.pepfar.gov/strategy.

Dr. Eric Goosby is the Ambassador for PEPFAR, Office of Global AIDS Coordinator. He described how the program is addressing prevention and treatment of HIV/AIDS among drug-using populations. He elaborated on the goals of PEPFAR's second 5-year strategy:

- Transitioning from emergency response to the promotion of sustainable country programs;
- Strengthening partner government capacity to lead the response to this epidemic and other health demands;
- Expanding prevention, care, and treatment in both concentrated and generalized epidemics;
- Integrating and coordinating HIV/AIDS programs with broader global health and development programs to maximize the impact on health systems; and
- Investing in innovation and operations research to evaluate impact, improve service delivery, and maximize outcomes.

Dr. Goosby referenced the fact that on July 30, 2008, the Tom Lantos and Henry J. Hyde United States Global Leadership against HIV/AIDS, Tuberculosis, and Malaria Reauthorization Act of 2008 was signed into law, authorizing up to $48 billion over 5 years to combat global HIV/AIDS, tuberculosis, and malaria. The reauthorization under Lantos-Hyde offers expanded opportunity and requests that U.S. Government programs fight HIV epidemics among IDUs by:

- Developing strategies to ensure the reduction of HIV infection; and
- Providing support services, such as substance abuse and treatment services.

Dr. Goosby presented data on the disease burden among IDUs with HIV in 13 selected PEPFAR countries that are heavily impacted. The countries included four in Asia, six in Central Asia and Eastern Europe, and three in Africa. In a total population of 2 billion, the estimated number of adults living with HIV/AIDS in these countries is 11 million, and 5.1 million are estimated to be IDUs living with HIV. In these countries, a greater percentage of IDUs living with HIV are males rather than females, but large numbers of women also are infected. There is a need to focus not only on needle and syringe exchange programs (NSPs) but on other comprehensive service linkages that will affect the health of mothers and children.

Dr. Goosby presented data on access to HIV prevention and treatment for IDUs in 10 countries receiving medication-assisted treatment (MAT) in the form of buprenorphine or methadone. The data included six countries from the former Soviet Union and four Asian countries. He noted that there has been a significant effort in China, resulting in some progress. He presented data on these countries with regard to the start-up of NSPs, which indicated that they were at the beginning stages of improving syringe availability and access. Dr. Goosby said it is too early to assess these efforts. The number of IDUs living with HIV/AIDS and receiving antiretroviral therapy (ART) in these countries is small; however, China is showing movement toward scaling up. He noted that the data collection systems are not robust, and there is a need to better understand how to mobilize the response and develop a unique dialogue in each country.

The planned PEPFAR prevention, treatment, and care activities for IDUs must face the significant challenges of closing the coverage gap, expanding access, and scaling up effective HIV core interventions. They plan to focus immediately on strategies that will increase the probability of success. PEPFAR must reach people within civil society—including unions, women's groups, and law enforcement—to help them understand how a comprehensive approach to prevention and treatment will minimize movement of the virus. The disease burden is high and growing, and the coverage rates for HIV core interventions are very low. The medical delivery system must capture individuals when they fall back into drug use and they must learn to expect relapse as part of recovery. Individuals should be linked with the full range of services they need, regardless of the difficulties of setting up and sustaining these services.

Dr. Goosby stated that the World Health Organization (WHO), the United Nations Office of Drugs and Crime (UNODC), and the Joint U.N. Programme on HIV/AIDS support the following comprehensive package of HIV services for IDUs:

- Community-based outreach;
- Needle and syringe programs;
- Opioid substitution therapy (OST) and other drug dependence treatment;
- HIV testing and counseling;

- Antiretroviral therapy;
- Prevention and treatment of sexually transmitted infections (STIs);
- Condom programs for IDUs and their sexual partners;
- Targeted information, education, and communication (IEC) for IDUs and their sexual partners;
- Vaccination, diagnosis, and treatment of viral hepatitis; and
- Prevention, diagnosis, and treatment of tuberculosis (TB).

The PEPFAR 5-year strategy aims to strengthen multilateral agency relationships and develop critical IDU "guiding principles" that will provide direction to PEPFAR country teams. Multilateral partners can provide important in-country technical support to IDU programs, bring significant resources to the table, and build political will for the inclusion of civil society in the process. PEPFAR is scaling up this effort under the umbrella of prevention. The Substance Abuse and Mental Health Services Administration (SAMHSA) and other Federal agencies are involved.

Because multilateral engagement is critical, PEPFAR is collaborating with U.N. agencies and other donors to support quality programming for IDUs:

- Multilateral organizations, such as UNAIDS, can use their in-country presence and government access to promote a rights- and evidence-based approach to prevention, care, and treatment;
- UNODC can work with law enforcement; and
- WHO can provide normative guidance.

Ambassador Goosby stated that it is important to focus on the epidemic, not on ideology. He said the principles guiding PEPFAR IDU programs are:

- Epidemiological and country-driven decisions;
- Structural interventions that facilitate implementation through supportive legislation, policies, and regulations;
- Evidence-based, comprehensive, and integrated HIV prevention, treatment, and care interventions for IDUs;
- Interventions implemented in a range of settings, including communities, jails, and prisons;
- Voluntary, equitable, and nondiscriminatory criteria for access to all services; and
- Interventions linked to standardized indicators for monitoring and evaluation of program impact.

PEPFAR is currently updating the comprehensive guidance for HIV prevention and treatment among IDUs, which includes technical considerations for implementing core interventions, including NSPs, medication-assisted therapy (MAT), and wraparound services and referrals that benefit IDUs. Dr. Goosby closed by stating that additional information is available at www.pepfar.gov.

Office of National AIDS Policy

The Office of National AIDS Policy (ONAP) is part of the White House Domestic Policy Council and is tasked with coordinating the continuing efforts of the government to reduce the number of HIV infections across the U.S. The Office emphasizes prevention through wide-ranging education initiatives and helps to coordinate the care and treatment of citizens with HIV/AIDS. In the U.S., important progress has been made in providing care and treatment to people living with HIV/AIDS, including housing and other essential supports, and in preventing new infections through reductions in the transmission rate of HIV. In addition, there have been important advances in the broad research agenda to find a cure, develop better treatments, and develop new interventions to prevent new infections.

ONAP coordinates with the National Security Council and the Office of the Global AIDS Coordinator, and works with international bodies to ensure that America's response to the global pandemic is fully integrated with other prevention, care, and treatment efforts around the world. Through the PEPFAR initiative, the U.S. has made progress in responding to the global HIV/AIDS pandemic, working with countries heavily affected by HIV/AIDS to help expand access to treatment, care, and prevention.

Mr. Jeffrey Crowley, Director of ONAP, stated that the President made a strong commitment to an effective national HIV/AIDS policy. He described how the Obama administration is refocusing on the domestic AIDS epidemic to reduce the number of new HIV infections, care for individuals with HIV and AIDS, and reduce HIV health disparities. ONAP conducted extensive information-gathering in meetings with youth, women, and experts on housing for people with HIV. They were in the synthesis phase, relying on interagency

working groups committed to tap into expertise across various Federal agencies. The work of these Federal partners is not limited to Department of Health and Human Services (HHS) agencies, such as the National Institutes of Health (NIH), the National Institute on Drug Abuse (NIDA), and SAMHSA; but includes the Departments of Labor, Justice, and others. ONAP is coordinating well with ONDCP, which has a separate but compatible strategy.

Mr. Crowley observed that HIV incidence has decreased in some drug-using populations in the U. S., but in some places, such as Puerto Rico, it has increased. The administration plans to ask key questions about these trends and will work to increase access to medical care for those with HIV. Health care reform is one part of this effort, but access to a broad range of other support services is also necessary. IDU populations need linkages to services that can address sexually transmitted infections, TB screening, prevention, and mental health services. The inequities in the U.S. health care system also raise racial and gender issues that must be addressed so that disparities can be reduced.

The President supports NSPs as a public health measure, and lifting the Federal funding ban on these programs was an important development in public health. ONAP is examining how they could move forward in a strategic way. The CDC and other relevant agencies have been asked to provide guidance on effective NSPS that are part of comprehensive HIV prevention programs.

Office of National Drug Control Policy

The White House Office of National Drug Control Policy, a component of the Executive Office of the President, was established by the Anti-Drug Abuse Act of 1988. The principal purpose of ONDCP is to establish policies, priorities, and objectives for the Nation's drug control program. The goals of the program are to reduce illicit drug use, manufacturing, and trafficking; drug-related crime and violence; and drug-related health consequences. To achieve these goals, the Director of ONDCP is charged with producing the National Drug Control Strategy. The Strategy directs the Nation's antidrug efforts and establishes a program, a budget, and guidelines for cooperation among Federal, State, and local entities. By law, the Director of ONDCP evaluates, coordinates, and oversees both the international and domestic antidrug efforts of executive branch agencies and ensures that such efforts sustain and complement State and local antidrug activities. The Director advises the President regarding changes in the organization, management, budgeting, and personnel of Federal agencies that could affect the antidrug efforts of the U.S. as well as Federal agencies' compliance with their obligations under the Strategy.

Dr. A. Thomas McLellan, Deputy Director, stated that ONDCP plans to work closely with other organizations addressing HIV/AIDS. He said that ONDCP is the only agency other than the Office of Management and Budget (OMB) with budget certification authority. This gives ONDCP the ability to ensure that budgets are compatible with the Office's strategy. ONDCP also communicates the administration's drug control policy to the public and takes the steps necessary to implement it.

A new strategy is being developed through consultation with 35 Federal agencies. Dr. McLellan noted that there have been tremendous developments in the knowledge of prevention, brief intervention, and recovery in recent years, and the new strategy will have a heightened emphasis on science-based decisions. Another priority area will be work at the community level, because that is where interventions are best administered.

ONDCP wants to remove barriers to access and is encouraging families and communities to learn how to support their members. The role of State governments and the Federal government will be to help communities take care of their own. ONDCP is calling for a national prevention network throughout the country in 30,000 communities that will learn how to implement evidence-based strategies. The grants currently issued by many agencies will be harmonized and awarded to communities that are best prepared to implement prevention. There also will be a greater emphasis on integrating prevention into mainstream health care; physicians and nurses must learn to conduct screenings and brief interventions. It is not possible for people to obtain safe and adequate

"The United States supports many specific interventions, such as medically-assisted drug treatment, syringe exchange programs as part of a comprehensive HIV/AIDS strategy leading to recovery, and the use of detoxification and treatment services tailored to the needs of those suffering from the disease of addiction."

ONDCP Director R. Gil Kerlikowske,
Opening Statement at the 53rd
U.N. Commission on Narcotic Drugs,
March 8, 2010

health care without considering substance use. It is hoped that the number of people in drug treatment will triple. This would reduce the costs the Nation already is incurring for care in emergency rooms.

ONDCP also plans to focus on populations most in need, such as adolescents—who can be reached with prevention efforts before problems start—and drug-related offenders. Most offenders enter the criminal justice system without having had substance abuse treatment. ONDCP is signaling an end to the "war on drugs," having learned that law enforcement alone cannot keep the country safe from drugs. Three decades of unprecedented science on drug prevention and treatment is available and should guide decision-making. Dr. McLellan closed by stating that mythologies must come to an end; our drug problems are made in the USA, not in other countries. He said it is critical to acknowledge and accept that responsibility.

National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, Centers for Disease Control and Prevention

The National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention (NCHHSTP) is responsible for public health surveillance, prevention research, and programs to prevent and control human immunodeficiency virus (HIV) infection and acquired immunodeficiency syndrome (AIDS), other sexually transmitted diseases (STDs), viral hepatitis, and tuberculosis (TB). Center staff work in collaboration with governmental and nongovernmental partners at community, State, national, and international levels, applying well-integrated multidisciplinary programs of research, surveillance, technical assistance, and evaluation.

Dr. Kevin Fenton, Director of NCHHSTP, noted the importance of looking at the intersection of drug use and HIV from a public health standpoint. He provided prevalence data on drug use in the U.S. based on the 2007 National Survey of Drug Use and Health (NSDUH).[1] He reported that 8% of the U.S. non-institutionalized population used illicit drugs in the past month, and this rate has been relatively stable since 2002. Prevalence was greatest among youth ages 18 to 20 years old, males, African Americans and Alaska Natives, and urban dwellers. In 2008, it was estimated that there were approximately 1.2 million IDUs in the U.S. using heroin, cocaine, and stimulants. Morbidity and mortality statistics indicate that substance abuse and drug addiction are among the leading causes of preventable mortality in the U.S. However, the risks for morbidity and mortality are highest with IDUs and include transmission of blood-borne infections by sharing non-sterile drug injection equipment and practicing unprotected vaginal or anal intercourse.

According to a recent *Journal of the American Medical Association (JAMA)* article,[2] IDUs accounted for 12% (6,600) of the estimated 56,300 new HIV infections in 2006. IDU/men who have sex with men (MSM) accounted for another 4% of new infections. The incidence of HIV among IDUs in the U.S. decreased by 80% between 1998–1990 and 2003–2006. People infected through injection drug use (204,000) accounted for 19% of the 1.1 million people living with HIV in 2006.[3] The distribution of AIDS cases in the U.S. is not random; there is geographic heterogeneity of high prevalence in the southern and northeastern regions, with lower numbers in the west. A disproportionate burden is experienced by African Americans.

Dr. Fenton emphasized that late HIV diagnosis among IDUs, particularly among males, is a significant problem. Many IDUs with newly diagnosed infections have suboptimal access to HAART and initiate therapy at more advanced stages of infection. Therefore, HIV testing should be a key component of any comprehensive strategy, and new opportunities to test IDUs should be considered in various settings (e.g., in correctional facilities and mental health clinics).[4]

The prevalence of hepatitis B is 800,000 to 1.2 million in the U.S. An estimated 43,000 new infections occurred in 2007. IDUs account for 15% of these new hepatitis B infections. Concerning hepatitis C, 3.2 million are chronically infected, with 17,000 new infections in 2007, and 12,000 deaths per year. Injection drug use is the main mode of transmission in the U.S. (48%), and 30% to 40% of HIV-positive persons are co-infected.[5]

In 2008, there was a 2.9% decrease in TB cases reported to the CDC (12,904 cases). Approximately one in five patients with TB is estimated to use an illicit drug, drink alcohol to excess, or both.[6-7] Studies indicate higher STD prevalence rates among some groups of people who use drugs, including persons who exchange sex for money, crack cocaine users, the incarcerated, and younger drug users. Syphilis among people who use drugs ranges from 1% to 6%; gonorrhea ranges from 1% to 3%.[8] The national prevalence of HSV-2 (herpes simplex virus-2) is 17%, but it is estimated that for those who use drugs, the rate is 38% to 61%.[9]

Data on HIV-associated risk behaviors from the National HIV Behavioral Surveillance System (NHBS) analyzed

interviews with 10,301 IDUs in 23 cities between May 2005 and February 2006.[10] The first wave of data indicated that 33% reported sharing syringes during the past 12 months; 63% had unprotected vaginal sex (highest among 18 to 24-year-olds). Sixty-six percent reported being tested for HIV in the previous 12 months. HCV testing was least common among those 18 to 24 years of age, and 72% of participants reported HCV testing or diagnosis at some time in their lives.

Dr. Fenton discussed the public health strategies that would help prevent and control HIV, hepatitis, STDs, and TB in persons who use drugs. These include:

- Identifying drug users through outreach and conducting risk assessments;
- Screening, diagnosis, and counseling;
- Treatment and vaccines;
- Managing persons with infections through prevention counseling, linkage to care, treatment adherence, and partner services;
- Prevention of mother-to-child transmission; and
- Reduction of risk behaviors among drug users through substance abuse treatment, syringe exchange programs, condoms, health education, and risk-reduction programs.

He noted the available resources at CDC on the issue, highlighting the "Compendium of Evidence-Based HIV Prevention Interventions," which was recently updated. It includes information on 69 interventions, including 15 for people who use drugs, 12 for IDUs specifically, and 8 that were tested with minority drug users.[11]

Dr. Fenton provided information on the status of the syringe exchange programs (SEPs) in operation in the U.S.[12] A total of 185 SEPs operate in 36 States, the District of Columbia, and Puerto Rico. They are authorized by state law in 14 states and by local governments in 3 states. There is free distribution of syringes not restricted by state law in 5 states. In 15 states, SEPs are operating without a claim to legality. Dr. Fenton said SEPs are a key part of the toolkit in the comprehensive approach to preventing HIV.

Concerning future approaches to HIV prevention for people who use drugs, CDC is working with Federal partners to develop guidance on the use of Federal funds to support SEPs consistent with fiscal year 2010 Congressional language and current programmatic guidance. CDC also is developing guidelines for integrated delivery of services for the prevention and control of HIV, viral hepatitis, STDs, and TB among drug users. This is intended to promote policy and organizational changes to foster program collaboration and service integration at venues that serve people who use drugs.

Dr. Fenton closed by remarking that the incidence of HIV among IDUs in the U.S. has decreased over the past two decades, but many challenges remain. CDC is working toward a more integrated approach to HIV and co-infection prevention.

Office of AIDS Research

The Office of AIDS Research (OAR), located within the National Institutes of Health Office of the Director, coordinates the scientific, budgetary, legislative, and policy elements of NIH AIDS research. OAR sets the trans-NIH scientific priorities for this large and diverse program, which is conducted or supported by nearly every NIH Institute and Center (ICs). OAR is enhancing collaboration and ensuring that research dollars are invested in the highest priority areas of scientific opportunity that will lead to new tools in the global fight against AIDS. To carry out this mission, OAR has authority to:

- Plan, coordinate, and evaluate the large, complex, and multifaceted NIH AIDS research portfolio;
- Develop an annual trans-NIH strategic plan for all HIV/AIDS research activities that guides the development of the AIDS research budget. The Trans-NIH Plan for HIV-Related Research is developed through a comprehensive, collaborative process involving representatives from NIH ICs and other Federal agencies; nongovernment experts from academia, foundations, and industry; and community representatives;
- Formulate the annual trans-NIH AIDS research budget;
- Review and approve IC initiatives to ensure that funds are provided for projects and initiatives with the highest scientific priority, eliminating duplication, and assuring cross-Institute collaboration;
- Develop an annual Presidential By-Pass budget for AIDS research based solely on scientific opportunity;
- Ensure that the NIH AIDS research portfolio is aligned with the highest priority AIDS research objectives, as

articulated in the Plan, by conducting annual portfolio analyses;

- Track and monitor all NIH AIDS expenditures by scientific area and Plan objective;
- Convene the Office of AIDS Research Advisory Council and its associated working groups, including those that develop Federal guidelines for treatment and prevention of HIV and its associated co-infections in adults, adolescents, and children; and
- Facilitate international AIDS research and training.

Dr. Jack Whitescarver, Director of OAR, explained that OAR functions as an "institute without walls," allowing NIH to pursue a unified research program to prevent and treat HIV infection and its associated complications. OAR does not issue grants. The Office has a national strategic plan that drives the budget, and NIH staff and outside experts help with the planning process. The areas that have been identified as requiring focused attention include:

- A prevention science initiative, including substance use;
- Comorbidities and complications;
- Genomics/genetics; and
- HIV-related disparities.

The Annual Trans-NIH Plan for HIV-Related Research (http://www.oar.nih.gov/strategicplan/) has the following overarching priorities:

- Reduce HIV incidence through microbicides, vaccines, behavioral and social science, and treatment as prevention;
- Improve disease outcomes through therapeutics;
- Reduce HIV-related disparities for women and girls and for racial and ethnic populations through research in international settings; and through training, infrastructure, and capacity building;
- Expand basic discovery research related to etiology and pathogenesis; and
- Translate research from the bench to the community using natural history studies, epidemiology, and information dissemination.

The reduction of HIV incidence through prevention science will require a combination of various biomedical and behavioral interventions. Demonstrated interventions include prevention of mother-to-child transmission (MTCT), circumcision, treatment for substance abuse, condoms, sterile syringes, and behavioral interventions. Key research areas include microbicides, behavioral and social science, vaccines, and treatment as prevention.

Areas of focus for the behavioral and social sciences include adherence/compliance issues; stigma, discrimination, poverty, and criminal justice issues; neurocognitive complications; drug and alcohol use and drug interactions; integrating research into the design and evaluation of interventions; and developing and testing innovative models and interventions that reflect the cultural and social contexts of the lives of racial and ethnic populations.

"Treatment as prevention" is a key approach to reducing HIV incidence. This includes reducing MTCT, post-exposure prophylaxis, and pre-exposure prophylaxis (PrEP); and using Seek, Test, and Treat to determine whether a community-wide testing program with immediate treatment can decrease the overall rate of new HIV infections in the community, including IDU populations.

A growing proportion of patients receiving therapy are demonstrating treatment failure and experiencing serious drug toxicities and side effects from ART, as well as co-infections. These include HCV, TB, malaria, HBV, and STIs. Patients also are at risk of malignancies; cardiovascular, neurological, and metabolic complications; diabetes and liver disease; and complications from premature aging. Improved disease outcomes are imperative.

The reduction of HIV-related disparities includes racial and ethnic disparities in the U.S., disparities between developed and resource-constrained nations, between men and women, between youth and older individuals, and those based on sexual identity. NIH will continue to place a high priority on understanding the causes of HIV-related health disparities, their role in disease transmission and acquisition, and their impact on treatment effectiveness and access. Research training programs for U.S. and international researchers are important for building the critical capacity to conduct AIDS research, both in U.S. racial and ethnic communities and in developing countries.

NIH also will continue its strong commitment to basic science, which is fundamental to its mission. Basic science provides the building blocks necessary to progress across all other scientific areas and to achieve the goals of the National HIV/AIDS Strategy.

Dr. Whitescarver addressed the translation of research from bench to bedside to community. A workshop on implementation science, held in 2009 in Cape Town, South Africa, was an important step in OAR's effort to develop a coordinated trans-NIH research agenda and strategy. The workshop provided an opportunity for researchers and implementers to debate a wide range of issues, including the definition of implementation science. Participants identified key opportunities for research and for changing the way implementation science is supported, organized, and utilized. Implementation science in health and HIV/AIDS was defined as:

- Comparisons between two or more established interventions;
- Comparisons of different approaches to delivering a health intervention;
- Strategies to encourage uptake of available services;
- Improved processes to guide implementation and program management;
- Adaptation of interventions to new populations and settings;
- Cost-effectiveness modeling; and
- Improved methodologies to implement interventions at scale.

The recommended research arising from the Implementation Science Workshop fell into five key areas:

- MTCT: Addressing implementation issues and barriers to coverage to optimize effectiveness;
- Engaging and retaining people in care: Testing models to optimize services, compare models of service provision and adherence support, define issues that result in suboptimal clinical outcomes, identify portals for HIV testing, and identify strategies that affect retention of pediatric and adolescent clients;
- Integration of other health care and HIV/AIDS services: Devising innovative approaches to integrating multiple services and determining where integration is advisable versus stand-alone approaches;
- HIV treatment as prevention, including among IDUs; and
- Optimal approaches for co-infections, including treatment of TB and drug use.

The full report from this meeting is available at http://www.pgaf.org/articles/pangaea-assists-implementation-science.html.

National Institute of Allergy and Infectious Diseases

The National Institute of Allergy and Infectious Diseases, an Institute within NIH, conducts and supports basic and applied research to better understand, treat, and ultimately prevent infectious, immunologic, and allergic diseases. To help turn the tide of the global HIV/AIDS pandemic, NIAID has established research collaborations with international colleagues in more than 50 countries to develop comprehensive approaches to the HIV pandemic encompassing vaccine development and other prevention activities, therapeutics, and care of the HIV-infected person. These collaborations already have yielded results, notably in developing methods to reduce mother-to-child transmission of HIV.

Dr. Anthony Fauci provided an overview of NIAID research on HIV/AIDS drug-using populations. He stated that natural history studies include: (1) the Multicenter AIDS Cohort Study (MACS), which is an ongoing prospective study of natural and treated histories of HIV-1 infection in homosexual and bisexual men conducted since 1984 by sites in four U.S. cities; and (2) the Women's Interagency HIV Study (WIHS), the largest observational cohort for studies of HIV/AIDS in women in the U.S. WIHS began in 1993, with centers in six cities. NIAID funds the core costs for the cohorts and NIDA funds the specific drug agenda.

MACS helped determine the role of non-prescribed recreational drugs in HIV transmission. Two articles on the subject were published in the *Journal of Acquired Immune Deficiency Syndromes* or JAIDS.[13-14]

The WIHS follow-up of approximately 3,800 HIV-positive and HIV-negative women indicated that many are current or former users of illicit drugs.[15] Selected areas of WIHS research include the impact of illicit drug use on:

- ART adherence and patterns of ART use;
- HIV pathogenesis and disease progression;
- Neuropsychological function and depression; and
- Kidney, liver, and cardiovascular disease.

Drug abuse programs, irrespective of modality, were associated with improved adherence to antiretroviral therapies among women drug users.[15]

Dr. Fauci noted six major NIAID-funded HIV/AIDS Clinical Trials Networks (CTNs):

- AIDS Clinical Trials Group (ACTG);
- HIV Prevention Trials Network (HPTN);
- HIV Vaccine Trials Network (HVTN);
- International Maternal Pediatric Adolescent AIDS Clinical Trials Group (IMPAACT);
- International Network for Strategic Initiatives in Global HIV Trials (INSIGHT); and
- Microbicide Trials Network (MTN).

Dr. Fauci listed the 30-plus FDA-approved antiretroviral drugs (ARVs) under the categories of Nucleoside/Nucleotide Reverse Transcriptase Inhibitors (NRTIs), Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs), Protease Inhibitors (PIs), Fusion Inhibitors, Entry Inhibitors, Integrase Inhibitors, and combinations (six combinations are available).

On the topic of HIV therapy among illicit drug users, Dr. Fauci stated that when they are not actively using drugs, adherence to and efficacy of ART among drug users is similar to other populations. However, there are special treatment challenges,[16] which include:

- Comorbid medical and mental health conditions;
- Limited access to HIV care;
- Inadequate adherence to therapy;
- Medication side effects and toxicities;
- Need for substance abuse treatment; and
- Drug interactions that can complicate HIV treatment.

Several HIV Prevention Trials Network (HPTN) studies target IDUs specifically:

- **HPTN 033:** Can high-risk populations, including IDUs, be recruited and retained?
- **HPTN 037:** Does peer educator intervention reduce HIV incidence among IDUs and members of a risk network?
- **HPTN 058:** Is long-term suboxone (buprenorphine + naloxone) substitution therapy for opiate addiction more effective than detoxification alone in preventing HIV infection and death among IDUs?

Dr. Fauci addressed pre-exposure prophylaxis, a well-established tool for preventing infectious diseases such as malaria. He stated that ARVs are proven to prevent mother-to-child HIV transmission and are useful as post-exposure prophylaxis. There is generally positive data in non-human primate models with tenofovir +/- emtricitabine, drugs with long half lives, good safety profiles, and a high genetic barrier to resistance (tenofovir). Because PrEP inhibits HIV without requiring a change in sexual habits, it is likely to have good acceptability.

Concerning the "test and treat" concept, Dr. Fauci cited an article by R.M. Granich et al.[17] He said the mathematical model described indicates that universal and annual voluntary HIV testing followed by immediate ART (irrespective of clinical stage or CD4 count) could reduce new HIV cases by 95% within 10 years. The concerns with such an effort would be the feasibility of this approach, protection of individual rights, drug resistance, toxicity, and financing.

General research issues relating to the "test and treat" concept that should be explored include universal testing, the relationship of the stage of HIV infection to efficiency of transmission, the efficacy of ART in preventing HIV transmission, drug resistance, behavioral "disinhibition," benefits to the individual, and cost-effectiveness for society.[18]

A new Request for Applications (RFA) was released on the Seek, Test, and Treat approach, which will address HIV in the criminal justice system. Applications were due April 1, 2010. NIDA, the National Institute of Mental Health (NIMH), and NIAID will commit $10.6 million to fund 7 to 10 new awards. Researchers are being encouraged to develop, implement, and test strategies to increase HIV testing and the provision of HAART to HIV-seropositive individuals involved with the criminal justice system, with a particular focus on continuity of HAART during and after community reentry following incarceration.

Dr. Fauci mentioned the first signal of efficacy in an HIV vaccine clinical trial in Thailand; the results were published online in the *New England Journal of Medicine*.[19] Building on the Thai vaccine trial, Dr. Fauci stated that the next generation of vaccines must achieve a 60% and 70% effect. He described the way forward for vaccines as:

- Determine the immune mechanisms that explain the findings in Thailand;
- Devise methods to optimize the immune responses that provided the protective effect;

- Based on knowledge of the immune mechanisms, evaluate new vaccine candidates to determine whether they provide better efficacy; and
- Assess IDU candidates after proof of concept is achieved in high-risk heterosexuals.

Dr. Fauci closed by describing comprehensive HIV prevention as education, condoms, STI treatment, testing/counseling, ARV therapy, drug/alcohol treatment, circumcision, microbicides, PrEP, harm reduction, and an effective vaccine.

United Nations Joint Programme on HIV/AIDS

UNAIDS, the Joint United Nations Programme on HIV/AIDS, is an innovative joint venture of the United Nations family, bringing together the efforts and resources of 10 UN system organizations in the AIDS response to help the world prevent new HIV infections, care for people living with HIV, and mitigate the impact of the epidemic. With its headquarters in Geneva, Switzerland, the UNAIDS Secretariat works on the ground in more than 80 countries worldwide. Action on AIDS by the UN system is coordinated in countries through the UN theme groups and the joint programs on AIDS. Cosponsors include the Office of the United Nations High Commissioner for Refugees (UNHCR), the United Nations Children's Fund (UNICEF), the World Food Programme (WFP), the United Nations Development Plan (UNDP), the United Nations Population Fund (UNFPA), the United Nations Office on Drugs and Crime (UNODC), the International Labor Organization (ILO), the United Nations Educational, Scientific, and Cultural Organization (UNESCO), the World Health Organization (WHO), and the World Bank. UNAIDS helps mount and support an expanded response to AIDS—one that engages the efforts of many sectors and partners from government and civil society.

Dr. Catherine Hankins, Chief Scientific Adviser to the United Nations Joint Programme on HIV/AIDS, described the division of labor in the Programme. She stated that UNAIDS, with 10 cosponsors, advocates and provides technical support to relevant government agencies and civil rights organizations to develop evidence-informed and human rights-based HIV policies and programming for IDUs. New initiatives include the ethical and participatory engagement of injection drug users in biomedical HIV prevention trials.

- **UNODC:** Lead role in relation to drug use. Specific focus areas: special needs of female drug users and training for law enforcement and prison staff.
- **WHO:** Supports implementation and scale-up of opioid substitution therapy and HIV treatment and care, including clinical protocol development and training.
- **World Bank:** Identifies IDU-related HIV prevention programming gaps; supports country programming, national and regional consultations financially.
- **UNICEF:** Programming guidance re: life skills and HIV prevention among injecting adolescents and support to prevent mother-to-child transmission among hard-to-reach drug-dependent pregnant women (e.g., CEE/CIS).
- **UNHCR:** Ensures harm-reduction services for refugees in Iran and Pakistan and returnees in Afghanistan.
- **UNDP, ILO, UNESCO, UNFPA, WFP:** Advocates and provides technical support in areas of comparative advantage.

Dr. Hankins also explained that UNODC is the lead agency in the UNAIDS family for HIV prevention and care among injection drug users and in prison settings. The Office is responsible for facilitating the development of a UN response to HIV that is associated with human trafficking. The focus of UNODC's work in these areas is to assist states in implementing large-scale, effective programs to prevent HIV infections and to provide care and support to people living with HIV; and to help states and civil society organizations develop and implement comprehensive HIV prevention and care programs for people who inject drugs. Dr. Hankins said the Reference Group to the UN on HIV and Injecting Drug Use was established in 2002 to provide technical advice on HIV and IDUs to UNODC, WHO, the UNAIDS Secretariat, and relevant cosponsors. It is an independent body of 24 experts from 20 countries.

Dr. Hankins provided data from the June 2009 UNAIDS Program Coordinating Board Meeting. She said it is estimated that there are IDUs in 148 countries (about 16 million people ages 15 to 64) and there is HIV among IDUs in 120 countries (3 million people). She highlighted the documents available from UNAIDS, including those on the topics of substitution therapy for opioid dependence, the framework for monitoring coverage, prevention in developing countries, and a declaration of commitment on HIV/AIDS. Dr. Hankins also described key milestones achieved by UNAIDS,

including a list of millennium goals for 2015, a 2006 political declaration on universal access, and the 2009 Commission on Narcotic Drugs Political Declaration Plan of Action.

Based on a UNAIDS report from September 2009, Dr. Hankins indicated the percentage of populations at high risk of HIV exposure that were reached with HIV prevention programs in numerous countries from 2005 to 2007. Of those reached, a large percentage of sex workers (60.4%) and men having sex with men (40.1%) reported knowing where they can receive an HIV test and that they were given condoms. Approximately 46% of injection drug users reported knowing where they could receive an HIV test and said they were given condoms, sterile injecting needles, and syringes.

In 2009, a joint effort by WHO/UNICEF/UNAIDS on universal access examined the need to scale up HIV prevention, treatment, and care in the health care sector. The report from this effort indicated that only 30 of the 92 low- and middle-income countries studied provided needle and syringe programs. The median number of syringes distributed annually by needle and syringe programs per IDU was 24.4 in Europe and Central Asia, and 26.5 in South and Southeast Asia. This is far below the internationally recommended target of 200 syringes per IDU per year. Only 26 countries reported providing opioid substitution therapy.

Dr. Hankins listed the main issues revealed by monitoring:

- Implementation of HIV prevention programs for people who inject drugs is suboptimal in low- and middle-income countries;
- Lack of non-discrimination laws and regulations is a major impediment to effective prevention programming;
- Monitoring and evaluation need to be strengthened, with better estimates of people in need, (denominators), indicators of the quality and intensity of HIV prevention activities, and completed guidelines developed by the UNAIDS Reference Group on operational monitoring and evaluation.

She described the World Bank Global HIV/AIDS Program (GHAP) "incidence model," which uses spreadsheets to analyze the distribution of infections based on major modes of transmission and calculates the expected incidence of HIV infection over the coming year. The model is based on the current prevalence of HIV infection, numbers of individuals with particular exposures, and the rates of exposures. It analyzes incidence in low-risk heterosexual sex and casual sex for those 15 to 24 years, 25+ years, and examines the effects of age mixing. The model allows analysts to see the role of IDUs in HIV infection in such countries as Mozambique, Kenya, Uganda, and Zambia.

In 2009, the UNAIDS Program Coordinating Board expressed the following concerns about HIV prevention among injection drug users:

- Low access to services;
- Inconsistencies across national and global policies;
- Resource shortages;
- Stigmatization and marginalization of drug users;
- Legal and policy restraints on opioid substitution therapy;
- Low access to hepatitis C diagnostics and treatment;
- Extremely low access to services in prisons;
- Improved identification of emerging epidemics; and
- Attention to drugs and HIV other than injecting.

Dr. Hankins closed by depicting the "HIV Prevention Crossroads," which included:

- Scale-up of effective strategies;
- Research for new biomedical, behavioral, and structural prevention strategies;
- New, "magic bullet" technologies; and
- Developing, implementing, and evaluating setting-appropriate combination prevention.

Conclusion

Panelists were in agreement that HIV/AIDS services globally have not kept pace with the current knowledge base on effective delivery of interventions. Even though the scientific knowledge and financial resources available to prevent and treat HIV/AIDS have expanded considerably over the last decade, the knowledge of how best to deliver proven interventions is lacking. This lack of translation of scientific knowledge into effective program implementation is referred to as the "implementation gap."[20]

The implementation gap has become a critical barrier in efforts to reduce HIV incidence and attain treatment and health outcome goals. In his presentation, Dr. Bruce

Schackman of Weill Cornell Medical College provided this definition of implementation science:

"Implementation science is the scientific study of methods to promote the integration of research findings and evidence-based interventions into health care policy and practice and, hence, to improve the quality and effectiveness of health services and care."

Dr. Schackman noted that establishing the field of implementation science will require forging collaborations between classic researchers and program implementers, identifying unique roles for lead organizations in global health delivery and research, and creating a strategic approach to identifying implementation research priorities.

The presentations of panelists and speakers at this meeting suggest that progress is being made toward these objectives and that a next step in the global HIV/AIDS effort is to use implementation science to positively impact public health and reduce the research-to-implementation gap.

References

[1] Substance Abuse and Mental Health Services Administration, Office of Applied Studies. Results from the 2007 National Survey on Drug Use and Health: National Findings. Rockville, MD, 2008. http://oas.samhsa.gov/nsduhLatest.htm

[2] Hall, H.I., Song, R., Rhodes, P., Prejean, J., An, Q., Lee, L.M., Karon, J., Brookmeyer, R., Kaplan, E.H., McKenna, M.T., & Janssen, R.S. Estimation of HIV incidence in the United States. *JAMA: Journal of the American Medical Association* 300(5), 520–529, 2008.

[3] HIV prevalence estimates—United States, 2006. *MMWR Morbidy and Mortality Weekly Report* 57, 1073–1076, 2008.

[4] HIV infection among injection-drug users – 34 states, 2004–2007. *MMWR Morbidity and Mortality Weekly Report* 58, 1291–1295, 2009.

[5] Daniels, D., Grytdal, S., & Wasley, A. Surveillance for acute viral hepatitis – United States, 2007. *MMWR Surveillance Summary* 58, 1–27, 2009.

[6] CDC. Reported Tuberculosis in the United States, 2008. Atlanta, GA: September 2009. http://www.cdc.gov/tb/statistics/reports/2008/default.htm

[7] Oeltmann, J.E., Kammerer, J.S., Pevzner, E.S., & Moonan, P.K. Tuberculosis and substance abuse in the United States, 1997–2006. *Archives of Internal Medicine* 169, 189–197, 2009.

[8] Semaan, S., Des Jarlais, D.C., & Malow, R. Behavior change and health-related interventions for heterosexual risk reduction among drug users. *Substance Use and Misuse* 41, 1349–1378, 2006.

[9] Xu, F., Sternberg, M.R., Kottiri, B.J., McQuillan, G.M., Lee, F.K., Nahmias, A.J., Berman, S.M., & Markowitz, L.E. Trends in herpes simplex virus type 1 and type 2 seroprevalence in the United States. *JAMA: Journal of the American Medical Association* 296, 964–973, 2006.

[10] HIV-associated behaviors among injecting-drug users–23 Cities, United States, May 2005–February 2006. *MMWR Morbidity and Mortality Weekly Report* 58, 329–332, 2009.

[11] CDC. 2009 Compendium of Evidence-Based HIV Prevention Interventions. Vol. 2010. Atlanta, GA: CDC, 2009. http://www.cdc.gov/hiv/topics/research/prs/evidence-based-interventions.htm

[12] Syringe exchange programs–United States, 2005. *MMWR Morbidity and Mortality Weekly Report* 56, 1164–1167, 2007.

[13] Ostrow, D.G., Plankey, M.W., Cox, C., Li, X., Shoptaw, S., Jacobson, L.P., & Stall, R.C. Specific sex drug combinations contribute to the majority of recent HIV seroconversions among MSM in the MACS. *Journal of Acquired Immune Deficiency Syndromes* 51, 349–355, 2009.

[14] Plankey, M.W., Ostrow, D.G., Stall, R., Cox, C., Li, X., Peck, J.A., & Jacobson, L.P. The relationship between methamphetamine and popper use and risk of HIV seroconversion in the multicenter AIDS cohort study. *Journal of Acquired Immune Deficiency Syndromes* 45, 85–92, 2007.

[15] Kapadia, F., Vlahov, D., Wu, Y., Cohen, M.H., Greenblatt, R.M., Howard, A.A., Cook, J.A., Goparaju, L., Golub, E., RIchardson, J., & Wilson, T. E. Impact of drug abuse treatment modalities on adherence to ART/HAART among a cohort of HIV seropositive women. *American Journal of Drug and Alcohol Abuse* 34, 161–170, 2008.

[16] Department of Health and Human Services. HHS treatment guidelines. 2009. http://www.aidsinfo.nih.gov/guidelines/Default.aspx?MenuItem=Guidelines&Search=On

[17] Granich, R.M., Gilks, C.F., Dye, C., De Cock, K.M., & Williams, B.G. Universal voluntary HIV testing with immediate antiretroviral therapy as a strategy for elimination of HIV transmission: A mathematical model. *Lancet* 373, 48–57, 2009.

[18] Dieffenbach, C.W. & Fauci, A.S. Universal voluntary testing and treatment for prevention of HIV transmission. *JAMA: Journal of the American Medical Association* 301, 2380–2382, 2009.

[19] Rerks-Ngarm, S., Pitisuttithum, P., Nitayaphan, S., Kaewkungwal, J., Chiu, J., Paris, R., Premsri, N., Namwat, C., de Souza, M., Adams, E., Benenson, M., Gurunathan, S., Tartaglia, J., McNeil, J.G., Francis, D.P., Stablein, D., Birx, D.L., Chunsuttiwat, S., Khamboonruang, C., Thongcharoen, P., Robb, M.L., Michael, N.L., Kunasol, P., Kim, J.H., & the MOPH-TAVEG Investigators. Vaccination with ALVAC and AIDSVAX to prevent HIV-1 infection in Thailand. *New England Journal of Medicine* 361, 2209–2220, 2009.

[20] Office of AIDS Research. Report From the Expert Consultation on Implementation Science Research: A Requirement for Effective HIV/AIDS Prevention and Treatment Scale-Up. Cape Town, South Africa, 2009. http://www.pgaf.org/articles/pangaea-assists-implementation-science.html.

Chapter 3. Comprehensive Approaches to HIV Prevention for People Who Use Drugs

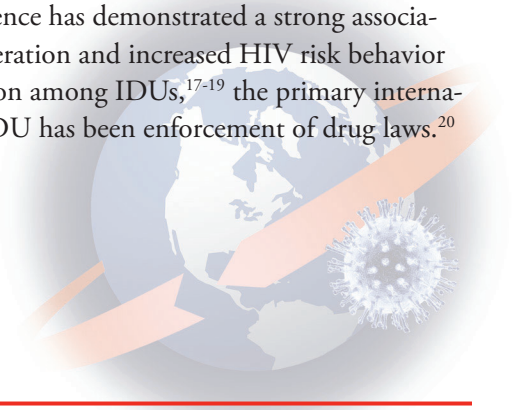
Substance use and abuse has been shown to be associated with an increased risk of HIV infection in key populations worldwide. HIV risk behavior is increased through the use of drugs during sex, sexual partnerships without condoms, and sex work. Injection drug use-related behavior is a significant factor contributing to HIV transmission, even though injection drug users (IDUs) constitute a very small proportion of the population. Globally, between 5% to 10% of HIV infections result from the sharing of contaminated injection equipment and drug preparations[1] although if sub-Saharan Africa is excluded, this percentage rises to about 30%.[2] Alcohol and noninjection drug use and HIV risk behaviors are prevalent in certain populations across the globe (e.g., alcohol use among heterosexuals in sub-Saharan Africa, club drug use among men who have sex with men).[3] In addition, substance use combines with other psychological issues and mental health disorders to help fuel the HIV epidemic.[4-5] Recent studies have found that substance use may have negative effects on HIV disease progression[6-7] and treatment outcomes because of reduced adherence and retention in care.[8-10]

In his presentation, Dr. Evan Wood of the British Columbia Centre for Excellence in HIV/AIDS addressed the need for comprehensive prevention strategies for preventing new HIV infections in diverse populations of drug users. He stated that in the absence of a vaccine or cure for AIDS, the most reliable and cost-effective approach for preventing new infections in these populations and their communities is the use of current, comprehensive prevention strategies.[11-12] Comprehensive HIV prevention includes a variety of complementary components, including drug abuse treatment, community-based outreach, and needle and syringe programs (NSPs). These strategies increase protective behaviors and reduce the risks for HIV/AIDS and other blood-borne infections, such as hepatitis B (HBV), hepatitis C (HCV), and other sexually transmitted diseases.

This chapter highlights the importance of including drug abusers—particularly IDUs—in comprehensive, multidisciplinary approaches to HIV prevention and treatment. The chapter describes the prevalence of HIV among IDUs, the relationship between HIV/AIDS and substance abuse, and outlines the challenges facing HIV-infected people who use drugs. It presents current strategies for prevention and treatment, and makes the case that effective substance abuse treatment is HIV prevention. Substance abuse treatment for injection drug users who use opioids is discussed in depth, and current information is provided on methamphetamines, other stimulants, club drugs, and alcohol abuse. Injection drug use is driving the HIV epidemics in Eastern Europe, Southeast and Central Asia, northern Africa, and the southern cone of South America[13], but only limited resources have been provided to stem IDU epidemics despite proven, evidence-based, effective interventions for IDUs.[14] Therefore, an emphasis is placed on comprehensive, integrated HIV prevention for this population.

The Case for Comprehensive HIV Prevention for Injection Drug Users

Injection drug use is a major international public health problem. Even though IDUs are known to be at a tremendously high risk of HIV infection, the level of global attention and resources directed toward evidence-based HIV prevention for this population remains inadequate.[15] Furthermore, although the past several decades have brought a wealth of knowledge regarding effective, evidence-based prevention programs for IDUs,[16] in many settings, non-evidence-based approaches receive greater attention and resources. For example, although a large body of evidence has demonstrated a strong association between incarceration and increased HIV risk behavior and HIV transmission among IDUs,[17-19] the primary international response to IDU has been enforcement of drug laws.[20]



HIV Prevalence among IDUs

Dr. Chris Beyrer of the Johns Hopkins Center for Public Health and Human Rights discussed HIV prevalence among IDUs at the meeting. Citing Mathers, et al. (2008),[21] he noted that:

- Injection drug use has been identified in 148 countries;
- An estimated 15.9 million people may inject drugs worldwide;
- The largest numbers of IDUs are in China, the U.S., and Russia (mid-estimates of HIV prevalence among IDUs are 12%, 16%, and 37%, respectively);
- HIV prevalence among injection drug users is 20 to 40% in five countries (Russia, Spain, Cambodia, Vietnam, and Libya) and over 40% in nine countries (Estonia, Ukraine, Burma, Indonesia, Thailand, Nepal , Argentina , Brazil, and Kenya; and
- Worldwide, about 3.0 million people who inject drugs may be HIV positive.

Dr. Beyrer stated that estimates of the number of people who inject drugs globally indicate that rates are highest in Eastern Europe and Central Asia.[21] He presented data on IDUs in those countries as a percentage of total registered HIV cases:

- 80% of cumulative region HIV infections are in IDUs;
- 62% of new infections in 2007 were in IDUs;
- Russia and the Ukraine have greater than 90% of all cases in the region, and greater than two-thirds are IDUs; and
- IDUs account for 60% of infections in Belarus, Georgia, Kazakhstan, Kyrgyzstan, Moldova, Russia, Ukraine, Tajikistan, and Uzbekistan.

Dr. Stephanie Srathdee of the University of California, San Diego, stated that there is growing concern about emerging epidemics of HIV among IDUs in sub-Saharan Africa against a backdrop in which HIV prevalence is already high (e.g., Nigeria, Kenya, Tanzania, and South Africa). Data suggest that there is considerable bridging between IDU and non-IDU populations through unprotected sex, which underscores the importance of studying bridging between these subgroups. Although the African epidemic still needs to be characterized, South African data suggest that it is an emerging epidemic. Data on the extent of injection drug use is not available for many countries in Africa, the Middle East, and Latin America.[21]

Dr. Strathdee noted that since the late 1980s, HIV incidence has declined by 80% among IDUs in the U.S.21 However, injection drug use continues to account for a substantial proportion of new HIV diagnoses, especially considering the indirect role injection drug use plays in heterosexual HIV transmission. In 2007, injection drug use was the third most frequently reported risk factor for HIV infection, after male-to-male sexual contact and high-risk heterosexual contact. Dr. Strathdee said that the most striking feature of the HIV epidemic among IDUs in the U.S. is racial disparities.[22] From 2004 to 2007, Blacks accounted for 57.5% of HIV-infected IDUs, Whites: 21.4%, Hispanics: 19.1%, American Indians or Alaska Natives: 0.6%, Asians: 0.4%, and Native Hawaiians or Other Pacific Islanders: 0.1%.

Effective HIV Programming

Effective HIV prevention programs have the potential to both prevent the spread of HIV among low-prevalence populations[23] and contain established epidemics.[24] Despite the wealth of evidence indicating the effectiveness of a large variety of HIV prevention programs, in many countries these interventions have yet to be adopted and implemented in an accessible and equitable manner.[25-26] To build consensus and improve universal access to these programs, the Joint United Nations Programme on HIV/AIDS (UNAIDS), UNODC, and the World Health Organization (WHO) recently published a joint technical guide for countries to set targets for universal access to HIV prevention, treatment, and care for injection drug users.[27] A critical element of this technical guide is the notion of comprehensiveness and integration to produce the most significant and sustained reductions in HIV risk behavior and infections.[28] The comprehensive package of HIV prevention, treatment, and care interventions for injection drug users recommended in the UNAIDS/UNODC/WHO technical guide include:

1. Needle and syringe programs (NSPs);
2. Opioid substitution therapy (OST) and other drug dependence treatment;
3. HIV counseling and testing;
4. Antiretroviral treatment (ART);
5. Sexually transmitted infection (STI) prevention and treatment;

6. Condom programming for IDUs and their partners;
7. Targeted information, education, and communication;
8. Vaccination, diagnosis, and treatment of viral hepatitis; and
9. Prevention, diagnosis, and treatment of TB.

Most of these interventions are described in detail in this report. However, a major focus of the consultation meeting was that expanding access to antiretroviral therapy is increasingly recognized as a highly effective HIV prevention strategy.[29-31] Recent mathematical modeling conducted by WHO has suggested that universal voluntary HIV testing in combination with immediate expansion of ART could largely eliminate the transmission of HIV within 10 years.[32] Given these findings, it is perhaps not surprising that both interventions (i.e., voluntary testing and ART) are recommended for IDU populations.[28] Furthermore, IDUs can successfully undergo HIV treatment, and systematic reviews have concluded that many IDUs can adhere to ART as well as non-IDU populations[33] and thus have been shown to benefit equally in terms of improved survival.[34] Given the unequivocal individual- and population-level health benefits of ART, universal access to HIV treatment for IDUs should be an international public health priority.

Integration of Services and Systems

Drug users and affected communities experience an evolving constellation of risk factors for HIV and other blood-borne pathogens.[25] To most effectively address these issues, evidence suggests that comprehensive, accessible, and culturally appropriate sets of preventive interventions are required.[35] Specifically, a large body of evidence suggests that when individual HIV prevention programs are combined, more significant and sustained reductions in risk can be achieved.[28] For example, a meta-analysis of behavioral risk reduction programs for IDUs concluded that interventions are most successful at reducing injection-related risks if they focus equally on drug- and sexual-related risk behaviors.[36] Since sexual risk behaviors often co-occur with injection-related risks,[37] NSPs and other harm reduction programs are more successful at preventing HIV transmission if safer sexual behavior counseling and condom provision are integrated into existing syringe exchange programs.[38-39]

Integrating other HIV prevention services within NSPs also has been shown to result in significant public health benefits. A prospective cohort study of IDUs in Amsterdam observed that NSP use was only associated with reductions in HIV and hepatitis C incidence when combined with participation in methadone therapy.[40] Offering motivational enhancement and contingency management (providing incentives for consecutive biological samples that prove abstinence) to active NSP users also has been shown to improve the likelihood of enrollment in substance abuse treatment.[41] It is clear that NSPs can successfully facilitate sustained contact between public health professionals and highly marginalized drug users and are therefore effective environments for rolling out other HIV prevention services. The successful integration of drug treatment services with other harm reduction programs also has been demonstrated. For example, the ability of supervised injecting facilities (SIFs) to reduce syringe sharing among attendants is unequivocal.[42] Furthermore, integrating addictions counseling within such facilities increases uptake of detoxification services.[43-44] The comprehensive delivery of services appears to have synergistic benefit in improving population-level health outcomes, including reduced HIV transmission among drug users.

The transmission of HIV from IDUs to their sexual partners through unprotected intercourse and other sexual HIV risk behaviors is well documented.[45-46] Therefore, sexual risk reduction interventions, including condom provision, STI testing, and improved access to other sexual health services, are an integral component of comprehensive prevention. A meta-analysis of behavioral programs targeting condom use has shown that such interventions are acceptable to IDUs and lead to sustained, albeit modest, decreases in sexual risk activity.[47] Although there is no one recommended set of components for effective sexual risk reduction interventions, programs based on multiple underlying theories and those focusing on role modeling, skills building, and enhancing social supports tend to be most effective.[48] It is important to note that these interventions do not need to operate independently from drug use-focused programming; for example, evaluations of two comprehensive educational interventions for drug-using women have shown significant reductions in measures of drug use frequency, syringe and equipment sharing, sex trade work, and unprotected intercourse.[49-50]

Effective HIV prevention should not only be comprehensive in terms of public health interventions but also should cut across sectors and involve organizations traditionally outside the health sector. The effective integration of law enforcement with health-focused programs often is considered critical in the development of successful HIV prevention interventions for IDUs.[51] Several authors have called for increased coordination of policing and public health initiatives to reduce

HIV transmission, emphasizing that these systems can work in concert rather than in an antagonistic manner. Further research is required to explore how these partnerships can best be achieved.[52-53]

Challenges of Drug-Using Populations

In the last two decades, syringe sharing among IDUs has contributed to an increasing proportion of new infections in many parts of the world such as Eastern Europe, East and Southeast Asia, and South America.[21] To examine the barriers and facilitators of HIV treatment among IDUs, Wood et al. reviewed information from published studies extracted from nine academic databases.[54] They noted that although current ART therapies have led to substantial reductions in HIV-related morbidity and mortality, clinical management of HIV disease presents major challenges.

Access to treatment is a major concern. Wood et al. found that even in settings in which HAART is widely available, IDUs have lower uptake than other HIV-infected populations. [54-55] Further, IDUs commonly present for HAART late in the course of HIV disease and often after AIDS-defining illnesses have developed.[10,56] The factors that explain poor access to treatment can be grouped into socio-structural, individual-level, and provider-based issues.[54] Socio-structural concerns result from national illicit drug strategies that use criminal sanctions to marginalize IDUs and create a "hidden population" that is difficult to reach with prevention and treatment services. Individual-level concerns include the perception by injection drug users that the side effects of HAART will be intolerable. There also is the specter of low self-efficacy, or doubt, about one's ability to adhere to HAART. Other individual-level factors that prevent access to HIV treatment include psychiatric illness, addiction-related instability, limited social support, and homelessness. Provider-based factors arise through physician reluctance to prescribe HAART to IDUs, even when they express an interest. Some physicians believe that IDUs will not adhere to HAART, that they will increase risk behaviors if they are treated, or that they will develop and transmit antiretroviral-resistant HIV. The latter assumption in particular is not supported by evidence.

A second set of barriers to HIV treatment among IDUs relates to adherence, with the most relevant socio-structural factor being incarceration. Individual barriers to adherence include the instability associated with high-intensity drug use, low self-efficacy, and the possible comorbidity of hepatitis C infection, which can increase the side effects of HAART and limit its tolerability. Provider issues concerning adherence relate to a lack of understanding of the social issues facing IDUs and geographic distance between providers and IDUs' residences. It is important to note, however, that studies have repeatedly demonstrated that many IDUs can manage high adherence to HAART. Further, ethical analyses have concluded that physicians should not withhold HAART from patients because they presume that they will be nonadherent.

A recent study by Uhlmann et al. (2010) supports the belief that drug users will initiate antiretroviral therapy and demonstrate high rates of subsequent adherence under certain conditions. The researchers studied a cohort of antiretroviral-naïve HIV-infected IDU to investigate whether exposure to methadone maintenance therapy (MMT) increased initiation and subsequent adherence to ART. The setting was Vancouver, British Columbia, where a province-wide antiretroviral dispensation program allowed for confidential records that provided accurate HIV-related outcomes, including the exact date of ART initiation and subsequent adherence. The study demonstrated that, among a community-recruited sample of antiretroviral-naïve opioid-using HIV-infected IDU, those who used MMT initiated ART at an elevated rate compared with those not receiving MMT. Additionally, those individuals on MMT had increased subsequent adherence to antiretroviral therapy. MMT appears to be an effective and underutilized strategy for increasing access to care. The researchers noted that active drug use should not be a contraindication to receiving ART, as MMT can offer improved adherence in this setting.[57]

In her presentation, Dr. Nora Volkow, Director of NIDA, acknowledged the barriers of access and adherence and presented the following strategies (adapted from[54]) to reduce them:

Socio-structural strategies:

- Low-threshold programs;
- Outreach services;
- Increased HIV testing;
- Reduced financial barriers; and
- Well-resourced prisons.

Individual strategies:

- Addiction treatment;
- Psychiatric treatment;
- Housing support; and
- Improved self-efficacy.

Provider-based strategies:

- Same-day appointments;
- On-site pharmacists;
- Interdisciplinary clinics;
- Adherence assistance;
- Daily observed therapy;
- Case management; and
- Greater HIV experience.

Additional strategies to address individual- and provider-based concerns are described by Wood et al.[54] They include improved health insurance coverage and free access to medical care. Relationships with HIV-experienced physicians can improve the self-efficacy of patients and increase their willingness to initiate HAART. Improvements in stability resulting from substance abuse treatment and housing support may help address physician reluctance to prescribe HAART. Several clinic characteristics have been associated with improved uptake and adherence to HAART. Delivery models that are highly flexible, comprehensive, and interdisciplinary are particularly helpful. Key features of such programs include on-site pharmacists, HIV specialist nurses, drop-in services, geographic proximity to home, and case management. An additional clinical consideration could be the co-administration of HAART with methadone maintenance or buprenorphine therapy. Medical knowledge of possible drug interactions is required to initiate such a strategy, however. Increased physician education on all aspects of HIV and substance abuse treatment, especially evidence-based delivery, has great potential to improve care. In general, any steps that can be taken to close the gap between drug users and the public health and medical systems will increase positive outcomes for the HIV-infected, drug-using population.

Furthermore, institutional, legal, and organizational responses can also significantly impact the success of comprehensive HIV prevention programs.[58] For example, a wealth of evidence indicates that specific policing practices, including "crackdowns," rarely result in decreased drug use, and in fact, can hinder HIV prevention efforts by displacing drug users out of the reach of public health services.[59-61] The arrest and incarceration of large numbers of drug users has generally failed to deter individuals from injecting drugs and reducing risk behavior.[62-63] Addressing structural barriers in settings of explosive IDU-driven epidemics (e.g., Russia, Ukraine) should be a key component in the provision and scale-up of universally accessible HIV prevention interventions in such areas.[64-65]

Interventions for Drug Using Populations

Since the mid-1980s, the U.S. National Institute on Drug Abuse (NIDA) has conducted extensive research on the effectiveness of intervention strategies to prevent the transmission of HIV in drug-using populations, particularly IDUs and crack cocaine users.[11] The complementary interventions that have been determined most useful in a comprehensive HIV/AIDS prevention approach are drug abuse treatment, syringe and needle exchange programs, community-based outreach, and testing and counseling services. These approaches are described in detail in the following paragraphs.

Substance Abuse Treatment

Drug abuse treatment is HIV prevention. As individuals reduce substance use, they often make healthy lifestyle changes, such as healthier relationships, better decisions about sexual behavior, and improved work habits. Those who engage in prosocial behavior during recovery increase their social networks with friends and family, which provides them with much-needed support and a buffer against substance use. For HIV-positive individuals, decisions about sexual behavior that are not influenced by intoxication reduce the likelihood of transmitting the virus to others and protect against infection from other diseases. In this way, substance abuse treatment functions as both secondary and primary prevention.[66-68]

Drug users who enter and continue in treatment are more likely than those who remain out of treatment to reduce risky activities, such as sharing needles and injection equipment or engaging in unprotected sex. Longitudinal studies that examined changes in HIV risk behaviors for patients in treatment found that longer retention and completion of treatment are correlated with reduction in HIV risk behaviors.[68] Drug abuse treatment can be conducted in a variety of settings (e.g., inpatient, outpatient, or residential) and often involves various approaches, including behavioral therapy, medications, or a combination of both. Evidenced-based treatment of substance abuse disorders is critical to HIV prevention and treatment

and other positive health outcomes among drug-using populations. Current methods of drug treatment are described in detail later in this chapter.

Community-Based Outreach

Community-based outreach is an effective approach for contacting drug users in their local neighborhoods to provide them with the means to change their risky drug- and sex-related behaviors. This approach relies on outreach workers who typically reside in the local community and are familiar with its drug use subculture. As a result, they are in a unique position to educate and influence their peers to stop using drugs and reduce their risks for HIV and other blood-borne infections. Outreach workers distribute HIV/AIDS educational information, bleach kits for disinfecting injection equipment when sterile equipment is not available, and condoms for safer sex. They also provide drug users with referrals for drug treatment, syringe access and exchange programs, and HIV, HBV, and HCV testing and counseling.

Community-based outreach is a highly effective method of accessing IDUs, and is thus considered a key factor in the successful delivery of many HIV prevention programs. Two comprehensive reviews of community-based outreach interventions provide strong evidence that these programs reach a significant proportion of high-risk IDUs and result in sustained reductions in HIV risk behavior. [69-70] Participation in outreach programs also has been shown to reduce the risk of HIV seroconversion among out-of-treatment IDUs.[71] Outreach-based interventions have been shown not only to reduce HIV risk among individuals but also among high-risk networks.[72-73] Given the considerable evidence indicating the success of community-based outreach programs, the importance and effectiveness of these interventions should not be understated.

Syringe and Needle Exchange Programs

Also known as needle exchange programs or syringe exchange programs (NEPs, or SEPs), needle and syringe programs (NSPs) complement community-based outreach and drug abuse treatment by providing drug users who will not or cannot seek treatment, or who are in treatment but continue to inject drugs, with access to sterile syringes and other services. These programs help remove potentially contaminated needles from circulation. They also serve as a bridge to active and out-of-treatment drug users by providing them with HIV/AIDS information and materials (e.g., bleach kits and condoms) to reduce their risks, by offering opportunities for HIV testing and counseling, and by providing referrals for drug abuse treatment and other social services. Hence, it is important that drug abuse treatment and other services are available and accessible to drug users referred by these programs.

Several landmark studies have demonstrated the ability of NSPs to reduce injection-related risk behavior[74] and HIV incidence[75] among IDUs who access these facilities. Furthermore, several reviews have concluded that overwhelming evidence exists to support the effectiveness, safety, and cost-effectiveness of these programs.[76-77] There is significant variation in the implementation and delivery of NSPs, particularly with regard to syringe availability and coverage. Programs with high-level coverage and less restrictive syringe dispensation policies are generally more effective at curtailing the spread of HIV than more restrictive programs[62,78] and are thus most strongly endorsed by WHO.[38]

Testing and Counseling Services and Linkages to Care

HIV testing and counseling services are an important part of comprehensive HIV prevention programs. These services are most effective when a range of anonymous and confidential testing options are available in diverse, accessible settings (e.g., mobile clinics) and at nontraditional times. The most current, rapid testing technologies can be especially useful. They allow drug users and others at risk to learn their test results as soon as they are available, plan a course of action to stop using drugs and reduce their risk of transmitting HIV to others, and obtain a referral to appropriate drug abuse and HIV treatment and other health services. Voluntary testing and linkage of HIV-positive individuals to ART treatment are recommended for IDU populations.[28] HIV testing and counseling staff also can inform drug users about their potential risks for contracting HBV and HCV and explain why it is important to be tested for these and other blood-borne and sexually transmitted infections. Staff members are trained to help people who test positive for HIV and/or other infections to inform their sex partners about their potential risks for infection and the importance of getting testing and counseling.

Substance Abuse Treatment as HIV Prevention

At the meeting, Dr. Charles O'Brien, University of Pennsylvania Department of Psychiatry, Center for Studies in Addiction, described current substance abuse treatments and their effectiveness in reducing the spread of HIV. Dr. O'Brien noted that effective substance abuse treatment prevents HIV infection and transmission because it:

- Reduces the frequency of illicit drug use;
- Results in fewer drug-related risk behaviors;
- Leads to fewer new infections; and
- Increases patient access to HIV treatment and primary care.

He noted that appropriate treatment of substance abuse disorders and HIV requires a comprehensive assessment of the disorder, any psychiatric and medical comorbidities, and engagement of relevant medical and social services. Medical treatment of substance abuse is frequently necessary to create sufficient patient stability prior to treating HIV and other comorbidities.

Substance Abuse Treatment Modalities

Drug addiction is a complex illness characterized by intense and, at times, uncontrollable drug craving, along with compulsive drug seeking and use that persist even in the face of devastating consequences.[79] While the path to drug addiction begins with the voluntary act of taking drugs, over time a person's ability to choose not to do so becomes compromised, and seeking and consuming the drug becomes compulsive. This behavior results largely from the effects of prolonged drug exposure on brain functioning. Addiction is a brain disease that affects multiple brain circuits, including those involved in reward and motivation, learning and memory, and inhibitory control over behavior.

Because drug abuse and addiction have so many dimensions and disrupt so many aspects of an individual's life, treatment is not simple. Effective treatment programs typically incorporate many components, each directed to a particular aspect of the illness and its consequences. Addiction treatment must help the individual stop using drugs, maintain a drug-free lifestyle, and achieve productive functioning in the family, at work, and in society. Because addiction is typically a chronic disease, people cannot simply stop using drugs for a few days and be cured. Most patients require long-term or repeated episodes of care to achieve the ultimate goal of sustained abstinence and recovery of their lives.

Opioid Treatment. Opioid substitution therapy (OST) programs involve the prescription of an opioid with similar action to the drug(s) used by the drug user, but with a lower degree of risk.[1] They are of two general types: detoxification programs, in which doses of the agonist will be reduced over time until a drug-free state has been reached; and substitution or maintenance programs, in which higher doses of the agonist are prescribed for longer time periods. Strong evidence indicates that OST suppresses illicit opioid use and decreases injection-related HIV risk behavior.[68,80] OST also is strongly associated with improved antiretroviral therapy adherence and better health outcomes among HIV-positive IDUs.[1] As described earlier in this chapter, a recently published study by Uhlmann et al. (2010) demonstrates that among a community-recruited sample of antiretroviral-naïve opioid-using HIV-infected IDU, those who used methadone maintenance therapy initiated ART at an elevated rate compared with those not receiving MMT.[57] Additionally, the individuals on MMT had increased subsequent adherence to antiretroviral therapy.

A systematic review published in the Cochrane Library concluded that OST reduces injection-related risk behavior and thus prevents HIV infections; however, only limited evidence was found to suggest an impact of OST on sexual risk behavior.[81] The agonist agent that has been most widely applied and researched for the treatment of opioid dependence is methadone. A single dose will prevent withdrawal for 24 hours.

Buprenorphine is increasingly being used as an alternative to methadone, with the exception of those who have the highest levels of heroin tolerance. Buprenorphine is a partial agonist, but it has enough morphine-like action to substitute for heroin, prevent withdrawal symptoms, and reduce craving. It can be administered less frequently than methadone and has less risk of overdose.[1] Because there is a risk of abuse, buprenorphine has been combined with naloxone—an opioid antagonist that is not active given orally—in the medication suboxone. If someone attempts to inject suboxone, the presence of the antagonist naloxone blocks feelings of euphoria. Dr. O'Brien pointed out that the partial agonist buprenorphine-naloxone combination offers new opportunities for treatment in HIV care settings.[82-83] OST programs provide a platform for HIV treatment and care, including the implementation of directly observed ART for opioid-dependent people living with HIV/AIDS, as well as care for opportunistic infections, such as tuberculosis.[28]

It is important to note that clinical case series and carefully controlled pharmacokinetic interaction studies have been conducted between methadone and most approved antiretroviral therapies. Important pharmacokinetic drug interactions have been demonstrated within each class of agents, affecting either methadone or antiretroviral agents. Few studies have been conducted with buprenorphine. Certain interactions between methadone and antiretroviral medications are known and may have important clinical consequences. To optimize

care, clinicians must be alert to these interactions and have a basic knowledge regarding their management.[84]

Naltrexone, an opioid antagonist, often is effective in highly motivated opioid-addicted populations, such as physicians, pharmacists, and nurses; parolees and probationers; and countries in which agonists are not available.[85-86] For the opioid-addicted population, outpatient treatment, drug-free counseling, and medication-free therapeutic communities are generally ineffective.

People who inject drugs are a small segment of the population, but they comprise a major part of the HIV-infected population. Neglecting the health of even a small segment of the community jeopardizes the public health. Research on opiate injectors has provided proof of concept that drug treatment is also HIV prevention. However, coverage of medication-assisted substance abuse treatment, including methadone and buprenorphine for opioid dependence, remains quite limited.[21] Research, implementation efforts, and strategies to expand access to OST are needed to combat the spread of HIV, especially in the developing world.

Alcoholism Treatment. People who use alcohol heavily tend to engage in risky behaviors, such as sex with multiple partners, unprotected vaginal and anal intercourse, and injection drug use.[87] A number of studies have examined the effect of various types of HIV prevention interventions and substance abuse treatment on high-risk sex and drug use behaviors in various cohorts of HIV-infected individuals, injection drug users, and persons engaging in heavy alcohol use.[47,68,88] Most studies found that these interventions can result in reduced sexual risk behaviors. The treatment settings ranged from day treatment to halfway houses, residential facilities, and methadone maintenance therapy.

Substance abuse modalities can be characterized as either pharmacological or psychosocial/behavioral in nature. Concerning pharmacological treatments, three medications have been FDA-approved for treating alcohol dependence: naltrexone, acamprosate, and disulfiram.[89] Naltrexone blocks opioid receptors that are involved in the rewarding effects of drinking and in the craving for alcohol. It reduces relapse to heavy drinking and is highly effective in some but not all patients—this is likely related to genetic differences. Acamprosate is thought to reduce symptoms of protracted withdrawal, such as insomnia, anxiety, restlessness, and dysphoria. It may be more effective in patients with severe dependence.[90] Disulfiram interferes with the degradation of alcohol, resulting in the accumulation of acetaldehyde, which produces an unpleasant reaction that includes flushing, nausea, and palpitations if the patient drinks alcohol. Compliance can be a problem, but for highly motivated patients, disulfiram can be very effective. A fourth, topiramate, is showing encouraging results in clinical trials. Used off label, it is effective, but has many side effects.[91]

Effective behavioral and psychosocial strategies for alcohol and other substance dependence problems include 12-step programs, such as Alcoholics Anonymous (AA), although new treatments are emerging.[92] Contingency management and cognitive behavioral strategies, including relapse prevention, have been demonstrated as feasible and effective for a variety of substance dependence problems. Cognitive behavioral therapy (CBT) is a broad set of psychological and educational techniques that provide substance-dependent individuals with critical knowledge about substance dependence and trainingin skills to promote abstinence.[93] Principles of CBT are integrated into most interventions for substance dependence in the U.S.. Motivational interventions, such as those developed by Miller and Rollnick, have shown promise, particularly for alcohol dependence.[94]

Treatment for Stimulants. Methamphetamine use plays a key role in morbidity and mortality rates among those with HIV infection or at risk of infection. Methamphetamine use by men who have sex with men (MSM) is approximately 10 times higher than in the general population.[95] Because methamphetamines increase sexual drive and decrease inhibitions, they are a driving force in HIV transmission. Most research on methamphetamine use and HIV risk behavior has focused on MSM populations, but sexual risk has also been documented among heterosexual populations of men and women.[96] Colfax and Shoptaw (2005) conducted a review of the literature to examine the influence of methamphetamine use on HIV transmission and HIV disease and made recommendations for treatment of methamphetamine users.[95] They found that behavioral counseling, either outpatient or inpatient, is the current standard of treatment. Most programs have been adapted from cocaine and alcohol programs and use motivational interviewing and cognitive-based therapy. However, dropout rates are high and relapse is very common. Contingency management (CM), pharmacologic interventions, and structural interventions (i.e., Federal regulation of sales) have met with moderate success. Contingency management involves the provision of vouchers or cash incentives for urine samples documenting drug abstinence. Strategies

using contingency management have been shown to be effective in increasing treatment retention, promoting drug abstinence, and reducing HIV risk behaviors.[97-99] A 2005 study compared the use of CBT plus contingency management with CBT-only, CM-only, and a tailored gay-specific CBT approach [(GCBT)-only] over a 1-year period with urban gay males who were methamphetamine-dependent to measure reductions in sexual risk behaviors.[93] Approximately half of the participants were infected with HIV. There were significant reductions in both methamphetamine use and sexual risk behaviors in all those who received treatment. A 2006 study of CM techniques to reduce HIV risk behaviors and improve adherence found that CM interventions have wide applicability to HIV prevention and management in clinical and community settings.[100] This is the case whether CM is implemented as stand-alone, or in combination with other interventions. However, long-term efficacy has yet to be demonstrated, and further research is needed.

Colfax and Shoptaw recommend that treatment providers ask all HIV-positive and at-risk patients about possible methamphetamine use. Those who report injection use should be provided with needle exchange referrals and discouraged from sharing needles or works. All sexually active methamphetamine users should be provided with HIV risk-reduction counseling with regard to sexual behavior, and condoms should be provided if necessary. Patients on ART should be assessed for adherence patterns and for medical comorbidities (e.g., skin infections, dental problems, depression). Patients should be referred to methamphetamine treatment programs if possible.

Treatment options for other stimulants, such as cocaine, are similar to methamphetamine and are based on outpatient counseling, particularly contingency management.[98] Behavioral interventions—including cognitive-behavioral therapy—also have been shown to be effective for decreasing cocaine use and preventing relapse. Treatment must be tailored to the individual patient's needs to optimize outcomes. This often involves a combination of treatment, social supports, and other services. Researchers are seeking to develop medications that help alleviate the severe craving associated with cocaine addiction, as well as medications that counteract cocaine-related relapse triggers, such as stress.[101] Currently there is no effective FDA-approved medication for stimulant addiction. Medications undergoing clinical trials include vigabatrin, topiramate, modafinil, and baclofen. A new vaccine to treat cocaine abuse is undergoing clinical trials.[102]

Club Drugs. Drugs that are frequently used in dance clubs or rave parties are known collectively as "club drugs." They include MDMA (methylenedioxymethamphetamine), also known as Ecstasy, ketamine, and GHB (gamma hydroxybutyrate); methamphetamines; and inhaled nitrites, known as "poppers." These drugs are frequently used among persons who are at risk for HIV infection or are infected with HIV. Most epidemiological data indicate that club drugs increase sexual behavior. Club drugs may interact with certain antiretroviral medications, and they have been associated with decreased adherence to medication regimens.[103] Club drug use is more prevalent among men who have sex with men compared with the general population. Few studies have evaluated the efficacy of approaches to treating the abuse of club drugs. Most research has focused on methamphetamine use (see previous subsection). The U.S. Centers for Disease Control and Prevention (CDC) currently is conducting a randomized, controlled group intervention for MSM who are substance users, including those who use club drugs. Called Project MIX, it will determine whether a risk-reduction approach will reduce substance use and risk behavior. At present there are no approved medications for club drug use. Clinicians should ask their patients about club drug use, counsel them about the risks associated with their use, and refer them to appropriate behavioral treatment when clinically indicated.[103]

HCV and TB Co-infection and Drug–Drug Interactions in Substance Users

Dr. Gerald Friedland from the Yale School of Medicine addressed comorbidities affecting drug users in the HIV-infected population. He explained that substance abusers were already at an increased risk of mortality and morbidity prior to the HIV epidemic. However, HIV/AIDS has had a devastating effect on drug-using populations worldwide. The epidemic has increased rates of a wide array of comorbid diseases, including: psychiatric/neurologic/drug related-complications; trauma; liver, renal, and pulmonary diseases; and infectious diseases. Although most of these were common among drug users prior to the HIV epidemic, their incidence, severity, and clinical presentation have been exacerbated by HIV infection. In both inpatient and outpatient substance abuse treatment settings, these diseases are more common than specific HIV-related complications, often confound both diagnosis and treatment, and are responsible for high rates of mortality.

This section focuses on the hepatitis C virus (HCV) and tuberculosis (TB), the two HIV co-infections with greatest

impact worldwide. HCV is of concern because an estimated 130 million people are infected worldwide:

- 2.7 million people are infected in the U.S. and 9 million in Western Europe;
- One-quarter to one-third of all HIV-infected persons are HCV infected;
- HCV infection incidence rates are in the range of 10–40/100 person years and occur earlier than HIV;[104]
- HCV prevalence rates are significantly higher among IDUs, approaching over 90% in some settings;[104-105]
- Chronic HCV produces hepatic inflammation resulting in eventual liver fibrosis, and in up to 50% of individuals, cirrhosis and end-stage liver disease (ESLD);[106]
- HIV co-infection accelerates progression of HCV and conveys a 6-fold relative risk (RR) of ESLD and a 2-fold RR of cirrhosis when compared with HCV mono-infection;[107]
- Factors contributing to accelerated fibrosis progression are low CD4 counts, lack of control of HIV replication, use of hepatotoxic drugs (including some antiretroviral medications), and frequent alcohol abuse; and
- Half of all liver transplantations are among patients with chronic viral hepatitis.[107]

Treatment for HCV is currently limited to the combination of pegylated interferon (PEG) and ribavirin (RBV), with a low success rate.[108] Treatment is prolonged and results in adverse side effects. In substance abusers, there often are intolerable neuropsychological and medical side effects and toxicities. As HAART among IDUs has reduced mortality, end-stage liver disease due to HCV/HIV co-infection has emerged as the leading cause of hospitalization and death related to HIV in the U.S. However, there are several new protease inhibitors and polymerase inhibitors for HCV that are in advanced- to late-stage clinical trials.

Unfortunately, there is limited uptake of HCV treatment by injection drug users. In 2005, a questionnaire on HCV treatment knowledge, experience, and barriers was administered to HCV-infected IDUs. Of 597 participants, 70% were aware that treatment was available, but only 22% understood that HCV could be cured, and a significant number refused treatment.[109] Mehta et al. proposed a framework for understanding the factors that affect utilization and adherence to HCV therapy among HCV mono-infected and HIV/HCV-co-infected IDUs.[110] They suggest that treatment needs can be assessed by liver biopsy, and therapy might be deferred in those with no liver disease and started in those with significant liver disease. Among those with moderate disease, further consideration of treatment advisability (medical factors that affect treatment response) and acceptability (individual, provider, and environmental barriers) would be needed before making treatment decisions. These factors are dynamic and should be continually evaluated.

TB is the most common AIDS-defining condition and the leading cause of death globally among those with HIV.[111] Drug use is associated with high rates of HIV and of TB infection and disease. In fact, substance abuse is the most commonly reported behavioral risk factor among patients with TB in the U.S. Patients who abuse substances are more contagious (e.g., smear positive) and remain contagious longer because treatment failure presumably extends periods of infectiousness.[112] Drug users are from two to six times more likely to contract TB than nonusers.[113] All-cause and TB-mortality rates are several-fold higher among drug users living with HIV than among others with HIV. Globally, 12 to 14 million persons are TB/HIV co-infected. Rehm J. et al. documented the association between alcohol use and TB. They found that there is a strong association between heavy alcohol use/alcohol use disorders (AUD) and TB. Heavy alcohol use strongly influences both the incidence and the outcome of the disease, and it was found to be linked to altered pharmacokinetics of medicines used in treatment of TB, social marginalization and drift, higher rate of re-infection, higher rate of treatment defaults, and development of drug-resistant forms of TB. Based on the available data, about 10% of the TB cases globally were estimated to be attributable to alcohol.[114]

The high rates of morbidity and mortality from TB among HIV-co-infected drug users is causing reactivation of latent TB infection and transmission of TB in congregate settings, such as prisons. In addition, there is a growing convergent epidemic of drug-resistant TB, multidrug-resistant (MDR) TB, and extensively drug-resistant (XDR) TB. MDR-TB is known to have resistance to isoniazid and rifampin, and requires a TB laboratory infrastructure for diagnosis. XDR-TB is extensively drug resistant; it is similar to MDR, with resistance to fluoroquinolones, and requires at least one injectable. It also requires a TB laboratory infrastructure for diagnosis.

Dr. Friedland defined acquired resistance and primary resistance. Acquired resistance is a result of treatment failure or a

consequence of program and/or patient limitations. It was the predominant mechanism seen in the past. Primary resistance results from transmission of resistant organisms. It is the predominant mechanism in areas of high HIV prevalence and is a consequence of increased susceptibility, rapid progression to disease, and absence of infection control. HIV-related MDR-TB outbreaks take place in industrialized countries and are characterized by HIV infection and rapid mortality. These types of TB epidemics have followed in the wake of rising HIV rates.

The treatment and prevention challenges of HIV, TB, and substance use include:

- Systems are vertical, inpatient, centralized, overburdened, and underfunded;[115]
- TB is difficult to treat with HIV co-infection;
- Treatment is prolonged for both TB and HIV;[84,116]
- Treatment is particularly difficult in drug-resistant TB. Second-line TB drugs are less potent, toxic, expensive, have limited availability, and 4-6 drugs are required for 18-24 months; and
- There are new drugs in the pipeline, but they are years away from approval.

In addition, individuals with HIV, TB, and substance use issues face a triple stigma and a lack of access to care. Medication adherence issues, additive toxicities, and drug-drug interactions complicate treatment, and there may be a need for M/XDR TB treatment as well.

Dr. Friedland also addressed drug-drug pharmacokinetic (PK) and pharmacodynamic (PD) interactions. The PK and PD interaction between rifampin, a TB treatment drug, and methadone has been known for more than 30 years. In 1976, Kreek et al. found that 21 out of 30 (70%) of opiate-addicted patients receiving methadone and being treated for TB developed symptoms and signs of opiate withdrawal, while 56 patients received non-rifampin TB regimens with no withdrawal symptoms.[117] Methadone plasma levels were 33%-68% lower during rifampin treatment. Since this initial interaction, the treatment of TB has been problematic among opiate-addicted patients. It is often either not suspected by clinicians or discounted. Treatment can result in clinical challenges, as TB and methadone programs are separate, with poor communication and no shared case management.

Concerning antiretroviral agents, TB and substance use therapies' drug interactions, pharmacologic (PK/PD) effects, and interactions with agents to treat the three diseases commonly occur. There are shared metabolic pathways (i.e., cytochrome P450 isoenzymes 3A4 and 2D6 metabolism). These may diminish the effectiveness of one, both, or all three therapies, by causing opiate withdrawal or overdose and/or increased toxicity or decreased antiretroviral and TB treatment efficacy. Antiretroviral and methadone/buprehorphine interactions include:[84,118-122]

- Increased AZT levels with methadone;
- Decreased ddI and D4T levels with methadone;
- Marked induction of methadone metabolism by efavirenz and nevirapine, with severe opiate withdrawal;
- Milder but unpredictable induction methadone metabolism by some protease inhibitors;
- Milder PK reduction in buprenorphine levels, but without PD effect; and
- Decreased methadone levels with raltegravir.

New directions in the area of drug-drug interactions include pharmacokinetic and pharmacodynamic studies with buprenorphine, examination of protease and integrase inhibitors, rifampin, and other rifamycins; and the use of buprenorphine and methadone. Studies are needed with second-line and new TB drugs, HCV drugs, and psychotropic drugs.

Prevention and treatment issues include increased the morbidity and mortality in IDUs as a result of these co-morbidities, as well as a number of special programmatic challenges, including the need for:

- Comprehensive and integrated programs and strategies;
- Reach-out to hidden populations;
- Integration and co-location of services (e.g., hospitals, HIV clinics, TB programs, prisons, drug treatment programs, community settings);
- Screening for and treatment of co-morbid conditions;
- Cross-training of staff; and
- The resources and the political will to implement necessary changes.

Future Directions

The evolving nature of the relationship between drug use and HIV transmission necessitate continual reform and innovation with respect to effective prevention strategies. For example, in both developed and transitioning countries, stimulants, including crack cocaine and methamphetamines, has increased dramatically.[123-127] Given the established relationship between HIV transmission and stimulant injection,[17] the development of tailored interventions for this population should be a priority.[128] Furthermore, although progress has been made in the treatment of individuals with stimulant dependence,[129] research in this area, including comprehensive psychosocial and substitution therapies are urgently required.

To respond rapidly and efficiently to emerging epidemics, the evaluation of novel interventions to reduce HIV transmission among drug users is critical. Once proven effective in one or more settings, these interventions should be implemented and evaluated in new environments.

However, there is growing acceptance of the ability of structural interventions to enact large-scale HIV risk behavior change. The fundamental tenet of this approach is to modify the social, structural, and physical environment in which drug use and HIV risk behavior co-occur.[62] For example, the provision of stable housing is increasing recognized as a highly effective structural intervention to reduce risk behavior and HIV transmission among people who use drugs.[130-132] Although empirical studies evaluating the effectiveness of structural interventions are clearly required, their nature and scope presents a number of research challenges.[133] The evaluation of "natural experiments" can also be an important means of identifying population-level impacts of structural interventions.

Additional recommendations for future directions in comprehensive prevention were made by breakout groups at the 2010 consultation meeting in the following areas: optimizing prevention modalities, drug abuse treatment as HIV prevention, HIV prevention and implementation, ART therapy as HIV prevention, human rights, HIV/AIDS treatment, and co-morbidity and adherence. All recommendations are found in appendix A.

Conclusion

In summary, even though leading international bodies have endorsed a variety of evidence-based interventions for HIV prevention among drug users, barriers to their delivery and implementation still exist. Furthermore, since sufficient levels of coverage and universal access are rare even in countries that provide some HIV prevention services for IDUs,[134] an international scale-up of coordinated sets of programs are required. As these individual programs are scaled up, it is important to consider the evidence that strongly indicates that comprehensive substance abuse treatment and prevention provides the greatest as yet unmet opportunity to reduce new HIV infections.

References

[1] Farrell, M., Gowing, L., Marsden, J., Ling, W., & Ali, R. Effectiveness of drug dependence treatment in HIV prevention. *International Journal of Drug Policy* 16, S67–S75, 2005.

[2] UNAIDS. Report on the Global AIDS Epidemic. 2006. http://www.unaids.org/en/KnowledgeCentre/HIVData/GlobalReport/2006/default.asp

[3] Van Tieu, H. & Koblin, B.A. HIV, alcohol, and noninjection drug use. *Current Opinion on HIV and AIDS* 4, 314–318, 2009.

[4] Kuehn, B.M. Integrated care needed for patients with HIV, drug abuse, and mental illness. *JAMA: Journal of the American Medical Association* 300, 494–495.

[5] Walkup, J., Blank, M.B., Gonzalez, J.S., Safren, S., Schwartz, R., Brown, L., Wilson, I., Knowlton, A., Lombard, F., Grossman, C., Lyda, K., & Schumacher, J. E. The impact of mental health and substance abuse factors on HIV prevention and treatment. *Journal of Acquired Immune Deficiency Syndromes* 47 Suppl 1, S15–19, 2008.

[6] Baum, M.K., Rafie, C., Lai, S., Sales, S., Page, B., & Campa, A.. Crack-cocaine use accelerates HIV disease progression in a cohort of HIV-positive drug users. *Journal of Acquired Immune Deficiency Syndromes* 50, 93–99, 2009.

[7] Cook, J.A., Burke-Miller, J.K., Cohen, M.H., Cook, R.L., Vlahov, D., Wilson, T.E., Golub, E.T., Schwartz, R.M., Howard, A.A., Ponath, C., Plankey, M.W., Levine, A.M., & Grey, D.D. Crack cocaine, disease progression, and mortality in a multicenter cohort of HIV-1 positive women. *AIDS* 22, 1355–1363, 2008.

[8] Celentano, D.D. & Lucas, G. Optimizing treatment outcomes in HIV-infected patients with substance abuse issues. *Clinical Infectious Diseases* 45 Suppl 4, S318–323, 2007.

[9] Kavasery, R., Galai, N., Astemborski, J., Lucas, G.M., Celetano, D.D., Kirk, G.D., & Mehta, S.H. Nonstructured treatment interruptions among injection drug users in Baltimore, MD. *Journal of Acquired Immune Deficiency Syndromes* 50, 360–366, 2009.

[10] Lert, F. & Kazatchkine, M.D. Antiretroviral HIV treatment and care for injecting drug users: An evidence-based overview. *The International Journal of Drug Policy* 18, 255–261, 2007.

[11] National Institute on Drug Abuse (NIDA). Principles of HIV/AIDS Prevention in Drug-Using Populations. http://archives.drugabuse.gov/POHP/index.html

[12] Parry, C.D., Petersen, P., Carney, T., & Needle, R. Opportunities for enhancing and integrating HIV and drug services for drug using vulnerable populations in South Africa. *The International Journal of Drug Policy.* Ahead of print, December 2009; In press.

[13] Vlahov, D., Robertson, A.M., & Strathdee, S.A. Prevention of HIV infection among injection drug users in resource-limited settings. *Clinical Infectious Diseases* 50 Suppl 3, S114–121, 2010.

[14] Needle, R. & Zhao, L. HIV Prevention Among Injection Drug Users. 2010. http://csis.org/publication/hiv-prevention-among-injection-drug-users.

[15] Joint United Nations Programme on HIV/AIDS (UNAIDS). *Report on the Global HIV/AIDS Epidemic 2008.* Geneva: UNAIDS, 2008. http://www.unaids.org/en/KnowledgeCentre/HIVData/GlobalReport/2008/

[16] Des Jarlais, D.C. & Semaan, S. HIV prevention for injecting drug users: The first 25 years and counting. *Psychosomatic Medicine* 70, 606–611, 2008.

[17] Tyndall, M.W., Currie, S., Spittal, P., Li, K., Wood, E., O'Shaughnessy, M.V., & Schechter, M. T. Intensive injection cocaine use as the primary risk factor in the Vancouver HIV-1 epidemic. *AIDS* 17, 887–893, 2003.

[18] Choopanya, K., Des Jarlais, D.C., Vanichseni, S., Kitayaporn, D., Mock, P.A., Raktham, S., Hireanras, K., Heyward, W.L., Sujarita, S., & Mastro, T.D. Incarceration and risk for HIV infection among injection drug users in Bangkok. *Journal of Acquired Immune Deficiency Syndromes* 29, 86–94, 2002.

[19] Zamani, S., Kihara, M., Gouya, M.M., Vazirian, M., Nassirimanesh, B., Ono-Kihara, M., Ravari, S.M., Safaie, A., & Ichikawa, S. High prevalence of HIV infection associated with incarceration among community-based injecting drug users in Tehran, Iran. *Journal of Acquired Immune Deficiency Syndromes* 42, 342–346, 2006.

[20] Wood, E., Werb, D., Marshall, B.D., Montaner, J.S., & Kerr, T. The war on drugs: A devastating public-policy disaster. *Lancet* 373, 989–990, 2009.

[21] Mathers, B.M., Deganhardt, L., Phillips, B., Wiessing, L., Hickman, M., Strathdee, S.A., Wodak, A., Panda, S., Tyndall, M., Toufik, A., Mattick, R.P., & the 2007 Reference Group to the UN on HIV and Injecting Drug Use. Global epidemiology of injecting drug use and HIV among people who inject drugs: A systematic review. *Lancet* 372, 1733–1745, 2008.

[22] HIV infection among injection-drug users—34 states, 2004–2007. *MMWR Morbidity and Mortality Weekly Report* 58, 1291–1295, 2009.

[23] Des Jarlais, D.C., Hagan, H., Friedman, S.R., Friedmann, P., Goldberg, D., Frischer, M., Green, S., Tunving, K., Ljunberg, B., & Wodak, A. Maintaining low HIV seroprevalence in populations of injecting drug users. *JAMA: Journal of the American Medical Association* 274, 1226–1231, 1995.

[24] Des Jarlais, C., Perlis, T., Friedman, S.R., Chapman, T., Kwok, J., Rockwell, R., Paone, D., Milliken, J., & Monterroso, E. Behavioral risk reduction in a declining HIV epidemic: Injection drug users in New York City, 1990–1997. *American Journal of Public Health* 90, 1112–1116, 2000.

[25] Metzger, D.S. & Navaline, H. HIV prevention among injection drug users: The need for integrated models. *Journal of Urban Health* 80, iii59–66, 2003.

[26] Mathers, B.M., Degenhardt, L., Ali, H., Wiessing, L., Hickman, M., Mattick, R.P., Myers, B., Ambekar, A., Strathdee, S.A., & the 2009 Reference Group to the UN on HIV and Injecting Drug Use. HIV prevention, treatment, and care services for people who inject drugs: A systematic review of global, regional, and national coverage. *Lancet* 375, 1014–1028, 2010.

[27] Donoghoe, M.C., Verster, A., Pervilhac, C., & Williams, P. Setting targets for universal access to HIV prevention, treatment and care for injecting drug users (IDUs): Towards consensus and improved guidance. *International Journal of Drug Policy* 19, S5–14, 2008.

[28] World Health Organization (WHO). WHO, UNODC, UNAIDS Technical Guide for Countries to Set Targets for Universal Access to HIV Prevention, Treatment and Care for Injecting Drug Users. Geneva: WHO, UNODC, UNAIDS, 2009. http://www.who.int/hiv/pub/idu/targetsetting/en/index.html

[29] Montaner, J.S., Hogg, R., Wood, E., Kerr, T., Tyndall, M., Levy, A.R., & Harrigan, P.R. The case for expanding access to highly active antiretroviral therapy to curb the growth of the HIV epidemic. *Lancet* 368, 531–536, 2006.

[30] Attia, S., Egger, M., Muller, M., Zwahlen, M., & Low, N. Sexual transmission of HIV according to viral load and antiretroviral therapy: Systematic review and meta-analysis. *AIDS* 23, 1397–1404, 2009.

[31] Wood, E., Kerr, T., Marshall, B.D., Li, K., Zhang, R., Hogg, R.S., Harrigan, P.R., & Montaner, J.S. Longitudinal community plasma HIV-1 RNA concentrations and incidence of HIV-1 among injecting drug users: Prospective cohort study. *British Medical Journal* 338, b1649, 2009.

[32] Granich, R.M., Gilks, C.F., Dye, C., De Cock, K.M., & Williams, B.G. Universal voluntary HIV testing with immediate antiretroviral therapy as a strategy for elimination of HIV transmission: A mathematical model. *Lancet* 373, 48–57, 2009.

[33] Donoghoe, M.C., Bollerup, A.R., Lazarus, J.V., Nielsen, S., & Matic, S. Access to highly active antiretroviral therapy (HAART) for injecting drug users in the WHO European Region 2002–2004. *International Journal of Drug Policy* 18, 271–280, 2007.

[34] Wood, E., Hogg, R.S., Lima, V.D., Kerr, T., Yip, B., Marshall, B.D., & Montaner, J. S. Highly active antiretroviral therapy and survival in HIV-infected injection drug users. *JAMA: Journal of the American Medical Association* 300, 550–554, 2008.

[35] Ball, A.L. HIV, injecting drug use and harm reduction: A public health response. *Addiction* 102, 684–690, 2007.

[36] Copenhaver, M.M., Johnson, B.T., Lee, I.C., Harman, J.J., & Carey, M.P. Behavioral HIV risk reduction among people who inject drugs: Meta-analytic evidence of efficacy. *Journal of Substance Abuse Treatment* 31, 163–171, 2006.

[37] Bogart, L.M., Kral, A.H., Scott, A., Anderson, R., Flynn, N., Gilbert, M.L., & Bluthenthal, R.N. Sexual risk among injection drug users recruited from syringe exchange programs in California. *Sexually Transmitted Diseases* 32, 27–34, 2005.

[38] World Health Organization (WHO). Guide to Starting and Managing Needle and Syringe Programmes. Geneva: WHO, 2007.

[39] Marshall, B.D., Wood, E., Zhang, R., Tyndall, M.W., Montaner, J.S., & Kerr, T. Condom use among injection drug users accessing a supervised injecting facility. *Sexually Transmitted Infections* 85, 121–126, 2009.

[40] Van Den Berg, C., Smit, C., Van Brussel, G., Coutinho, R., & Prins, M. Full participation in harm reduction programmes is associated with decreased risk for human immunodeficiency virus and hepatitis C virus: Evidence from the Amsterdam Cohort Studies among drug users. *Addiction* 102, 1454–1462, 2007.

[41] Kidorf, M., King, V.L., Neufeld, K., Peirce, J., Kolodner, K., & Brooner, R.K. Improving substance abuse treatment enrollment in community syringe exchangers. *Addiction* 104, 786–795, 2009.

[42] Milloy, M.J. & Wood, E. Emerging role of supervised injecting facilities in human immunodeficiency virus prevention. *Addiction* 104, 620–621, 2009.

[43] Wood, E., Tyndall, M.W., Zhang, R., Stoltz, J.A., Lai, C., Montaner, J.S., & Kerr, T. Attendance at supervised injecting facilities and use of detoxification services. *New England Journal of Medicine* 354, 2512–2514, 2006.

[44] Wood, E., Tyndall, M.W., Zhang, R., Montaner, J.S., & Kerr, T. Rate of detoxification service use and its impact among a cohort of supervised injecting facility users. *Addiction* 102, 916–919, 2007.

[45] Kral, A.H., Bluthenthal, R.N., Lorvick, J., Gee, L., Bacchetti, P., & Edlin, B.R. Sexual transmission of HIV-1 among injection drug users in San Francisco, USA: Risk-factor analysis. *Lancet* 357, 1397–1401, 2001.

[46] Strathdee, S.A. & Sherman, S.G. The role of sexual transmission of HIV infection among injection and non-injection drug users. *Journal of Urban Health* 80, iii7–14, 2003.

[47] Semaan, S., Des Jarlais, D.C., Sogolow, E., Johnson, W.D., Hedges, L.V., Ramirez, G., Flores, S.A., Norman, L., Sweat, M.D., & Needle, R. A meta-analysis of the effect of HIV prevention interventions on the sex behaviors of drug users in the United States. *Journal of Acquired Immune Deficiency Syndromes* 30, S73–93, 2002.

[48] Des Jarlais, D. & Semaan, S. Interventions to reduce the sexual risk behaviour of injecting drug users. *International Journal of Drug Policy* 16, S58–S66, 2005.

[49] Sterk, C.E., Theall, K.P., Elifson, K.W., & Kidder, D. HIV risk reduction among African-American women who inject drugs: A randomized controlled trial. *AIDS and Behavior* 7, 73–86, 2003.

[50] Wechsberg, W.M., Lam, W.K., Zule, W.A., & Bobashev, G. Efficacy of a woman-focused intervention to reduce HIV risk and increase self-sufficiency among African American crack abusers. *American Journal of Public Health* 94, 1165–1173, 2004.

[51] Hammett, T.M., Bartlett, N.A., Chen, Y., Ngu, D., Cuong, D.D., Phuong, N.M., Tho, N.H., Van, L.K., Liu, W., Donghua, M., Shaomi, X., Chen, H., Quyen, H.N., Broadhead, R.S., & Des Jarlais, D.C. Law enforcement influences on HIV prevention for injection drug users: Observations from a cross-border project in China and Vietnam. *International Journal of Drug Policy* 16, 235–245, 2005.

[52] DeBeck, K., Wood, E., Zhang, R., Tyndall, M., Montaner, J., & Kerr, T. Police and public health partnerships: Evidence from the evaluation of Vancouver's supervised injection facility. *Substance Abuse Treatment, Prevention, and Policy* 3, 11, 2008.

[53] Hammett, T.M., Wu, Z., Duc, T.T., Stephens, D., Sullivan, S., Liu, W., Chen, Y., Ngu, D., & Des Jarlais, D.C. "Social evils" and harm reduction: The evolving policy environment for human immunodeficiency virus prevention among injection drug users in China and Vietnam. *Addiction* 103, 137–145, 2008.

[54] Wood, E., Kerr, T., Tyndall, M.W., & Montaner, J.S. A review of barriers and facilitators of HIV treatment among injection drug users. *AIDS* 22, 1247–1256, 2008.

[55] Chander, G., Himelhoch, S., Fleishman, J.A., Hellinger, J., Gaist, P., Moore, R.D., & Gebo, K.A. HAART receipt and viral suppression among HIV-infected patients with co-occurring mental illness and illicit drug use. *AIDS Care* 21, 655–663, 2009.

[56] Grigoryan, A., Hall, H.I., Durant, T., & Wei, X. Late HIV diagnosis and determinants of progression to AIDS or death after HIV diagnosis among injection drug users, 33 US States, 1996–2004. *PLoS One* 4, e4445, 2009.

[57] Uhlmann, S., Milloy, M.J., Kerr, T., Zhang, R., Guyillemi, S., Marsh, D., Hogg, R.S., Montaner, J.S., & Wood, E. Methadone maintenance therapy promotes initiation of antiretroviral therapy among injection drug users. *Addiction*, 2010.

[58] Rhodes, T., Singer, M., Bourgois, P., Friedman, S.R., & Strathdee, S.A. The social structural production of HIV risk among injecting drug users. *Social Science & Medicine* 61, 1026–1044, 2005.

[59] Wood, E., Spittal, P.M., Small, W., Kerr, T., Li, K., Hogg, R.S., Tyndall, M.W., Montaner, J.S., & Schehter, M.T. Displacement of Canada's largest public illicit drug market in response to a police crackdown. *Canadian Medical Association Journal* 170, 1551–1556, 2004.

[60] Bluthenthal, R.N., Kral, A.H., Lorvick, J., & Watters, J.K. Impact of law enforcement on syringe exchange programs: A look at Oakland and San Francisco. *Medical Anthropology* 18, 61–83, 1997.

[61] Burris, S., Blankenship, K.M., Donoghoe, M., Sherman, S., Vernick, J.S., Case, P., Lazzarini, Z., & Koester, S. Addressing the "risk environment" for injection drug users: The mysterious case of the missing cop. *Milbank Quarterly* 82, 125–156, 2004.

[62] Des Jarlais, D.C. Structural interventions to reduce HIV transmission among injecting drug users. *AIDS* 14, S41–46, 2000.

[63] Friedman, S.R., Cooper, H.L., Tempalski, B., Keem, M., Friedman, R., Flom, P.L., & Des Jarlais, D.C. Relationships of deterrence and law enforcement to drug-related harms among drug injectors in US metropolitan areas. *AIDS* 20, 93–99, 2006.

[64] Tkatchenko-Schmidt, E., Renton, A., Gevorgyan, R., Davydenko, L., & Atun, R. Prevention of HIV/AIDS among injecting drug users in Russia: Opportunities and barriers to scaling-up of harm reduction programmes. *Health Policy* 85, 162–171, 2008.

[65] Aceijas, C., Hickman, M., Donoghoe, M.C., Burrows, D., & Stuikyte, R. Access and coverage of needle and syringe programmes (NSP) in Central and Eastern Europe and Central Asia. *Addiction* 102, 1244–1250, 2007.

[66] Bruce, R.D. Methadone as HIV prevention: High volume methadone sites to decrease HIV incidence rates in resource limited settings. *The International Journal of Drug Policy* 21, 122–124, 2010.

[67] Farrell, M., Gowing, L., Marsden, J., Ling, W., & Ali, R. Effectiveness of drug dependence treatment in HIV prevention. *The International Journal of Drug Policy* 16S, S67–S75, 2005.

[68] Sorensen, J.L. & Copeland, A.L. Drug abuse treatment as an HIV prevention strategy: A review. *Drug and Alcohol Dependence* 59, 17–31, 2000.

[69] Coyle, S.L., Needle, R.H. & Normand, J. Outreach-based HIV prevention for injecting drug users: A review of published outcome data. *Public Health Reports* 113, 19–30, 1998.

[70] Needle, R.H., Burrows, D., Friedman, S.R., Dorabjee, J., Touze, G., Badrieva, L., Grund, J-P.C., Kumar, M.S., Nigro, L., Manning, G., & Latkin, C. Effectiveness of community-based outreach in preventing HIV/AIDS among injecting drug users. *International Journal of Drug Policy* 16, 45–57, 2005.

[71] Wiebel, W.W., Jimenez, A., Johnson, W., Ouellet, L., Jovanovic, B., Lampinen, T., Murray, J., & O'Brien, M.U. Risk behavior and HIV seroincidence among out-of-treatment injection drug users: A four-year prospective study. *Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology* 12, 282–289, 1996.

[72] Latkin, C.A., Sherman, S., & Knowlton, A. HIV prevention among drug users: Outcome of a network-oriented peer outreach intervention. *Health Psychology* 22, 332–339, 2003.

[73] Latkin, C.A. Outreach in natural settings: The use of peer leaders for HIV prevention among injecting drug users' networks. *Public Health Reports* 113, 151–159, 1998.

[74] Bluthenthal, R.N., Kral, A.H., Gee, L., Erringer, E.A., & Edlin, B.R. The effect of syringe exchange use on high-risk injection drug users: A cohort study. *AIDS* 14, 605–611, 2000.

[75] Des Jarlais, D.C., Marmor, M., Paone, D., Titus, S., Shi, Q., Perlis, T., Jose, B., & Friedman, S.R. HIV incidence among injecting drug users in New York City syringe-exchange programmes. *Lancet* 348, 987–991, 1996.

[76] Wodak, A. & Cooney, A. Do needle syringe programs reduce HIV infection among injecting drug users: A comprehensive review of the international evidence. *Substance Use & Misuse* 41, 777–813, 2006.

[77] Gibson, D.R., Flynn, N.M., & Perales, D. Effectiveness of syringe exchange programs in reducing HIV risk behavior and HIV seroconversion among injecting drug users. *AIDS* 15, 1329–1341, 2001.

[78] Bluthenthal, R.N., Anderson, R., Flynn, N.M., & Kral, A.H. Higher syringe coverage is associated with lower odds of HIV risk and does not increase unsafe syringe disposal among syringe exchange program clients. *Drug and Alcohol Dependence* 89, 214–222, 2007.

[79] National Institute on Drug Abuse (NIDA). Treatment Research. http://www.nida.nih.gov/PODAT/PODATIndex.html

[80] Metzger, D.S., Navaline, H., & Woody, G.E. Drug abuse treatment as AIDS prevention. *Public Health Reports* 113, 97–106, 1998.

[81] Gowing, L., Farrell, M., Bornemann, R., Sullivan, L.E., & Ali, R. Substitution treatment of injecting opioid users for prevention of HIV infection (Review). *Cochrane Database of Systematic Reviews* Issue 2, Art. No.: CD004145. DOI: 004110.001002/14651858.CD14004145.pub14651853, 2008.

[82] Schottenfeld, R.S., Chawarski, M.C., & Mazlan, M. Maintenance treatment with buprenorphine and naltrexone for heroin dependence in Malaysia: A randomised, double-blind, placebo-controlled trial. *Lancet* 371, 2192–2200, 2008.

[83] Sullivan, L.E., Moore, B.A., Chawarski, M.C., Pantalon, M.V., Barry, D., O'Connor, P.G., Schottenfeld, R.S., & Fiellin, D.A. Buprenorphine/naloxone treatment in primary care is associated with decreased human immunodeficiency virus risk behaviors. *Journal of Substance Abuse Treatment* 35, 87–92, 2008.

[84] Bruce, R.D., Altice, F.L., Gourevitch, M.N., & Friedland, G.H. Pharmacokinetic drug interactions between opioid agonist therapy and antiretroviral medications: Implications and management for clinical practice. *Journal of Acquired Immune Deficiency Syndromes* 41, 563–572, 2006.

[85] Krupitsky, E.M., Zvartau, E.E., Masalov, D.V., Tsoy, M.V., Burakov, A.M., Egorova, V.Y., Didenko, T.Y., Romanova, T.N., Ivanova, E.B., Bespalov, A.Y., Verbitskaya, E.V., Neznanov, N.G., Grinenko, A.Y., O'Brien, C.P., & Woody, G.E. Naltrexone with or without fluoxetine for preventing relapse to heroin addiction in St. Petersburg, Russia. *Journal of Substance Abuse Treatment* 31, 319–328, 2006.

[86] Patapis, N.S. & Nordstrom, B.R. Research on naltrexone in the criminal justice system. *Journal of Substance Abuse Treatment* 31, 113–115, 2006.

[87] Palepu, A., Raj, A., Horton, N.J., Tibbetts, N., Meli, S., & Samet, J. H. Substance abuse treatment and risk behaviors among HIV-infected persons with alcohol problems. *Journal of Substance Abuse Treatment* 28, 3–9, 2005.

[88] Woods, W.J., Guydish, J.R., Sorensen, J.L., Coutts, A., Bostrom, A., & Acampora, A. Changes in HIV-related risk behaviors following drug abuse treatment. *AIDS* 13, 2151–2155, 1999.

[89] (NIDA), N.I.o.D.A. NIDA InfoFacts: Treatment Approaches for Drug Addiction. http://www.nida.nih.gov/infofacts/treatmeth.html

[90] Olive, M.F. Pharmacotherapies for alcoholism: The old and the new. *CNS and Neurological Disorders Drug Targets* 9, 2–4, 2010.

[91] Kenna, G.A., Lomastro, T.L., Schiesl, A., Leggio, L., & Swift, R.M. Review of topiramate: An antiepileptic for the treatment of alcohol dependence. *Current Drug Abuse Review* 2, 135–142, 2009.

[92] Shoptaw, S. & Frosch, D.L. Substance Abuse Treatment as HIV Prevention for Men Who Have Sex with Men. *AIDS and Behavior* 4, 193–203, 2000.

[93] Shoptaw, S., Reback, C.J., Peck, J.A., Yang, X., Rotheram-Fuller, E., Larkins, S., Veniegas, R.C., Freese, T.E., & Hucks-Ortiz, C. Behavioral treatment approaches for methamphetamine dependence and HIV-related sexual risk behaviors among urban gay and bisexual men. *Drug Alcohol Dependence* 78, 125–134, 2005.

[94] Miller, W. & Rollnick, S. *Motivational Interviewing: Preparing People to Change Addictive Behavior.* New York: Guilford Press, 1991.

[95] Colfax, G. & Shoptaw, S. The methamphetamine epidemic: Implications for HIV prevention and treatment. *Current HIV/AIDS Report* 2, 194–199, 2005.

[96] Semple, S.J., Grant, I., & Patterson, T.L. Female methamphetamine users: Social characteristics and sexual risk behavior. *Women and Health* 40, 35–50, 2004.

[97] Ghitza, U.E., Epstein, D.H., & Preston, K.L. Contingency management reduces injection-related HIV risk behaviors in heroin and cocaine using outpatients. *Addictive Behavior* 33, 593–604, 2008.

[98] Hanson, T., Alessi, S.M., & Petry, N.M. Contingency management reduces drug-related human immunodeficiency virus risk behaviors in cocaine-abusing methadone patients. *Addiction* 103, 1187–1197, 2008.

[99] Shoptaw, S., Klausner, J.D., Reback, C.J., Tierney, S., Stansell, J., Hare, C.B., Gibson, S., Siever, M., King, W.D., Kao, U., & Dang, J. A public health response to the methamphetamine epidemic: The implementation of contingency management to treat methamphetamine dependence. *BMC Public Health* 6, 214, 2006.

[100] Haug, N.A. & Sorensen, J.L. Contingency management interventions for HIV-related behaviors. *Current HIV/AIDS Report* 3, 154–159, 2006.

[101] National Institute on Drug Abuse (NIDA). NIDA InfoFacts: Cocaine. http://www.nida.nih.gov/infofacts/cocaine.html

[102] Gao, Y., Orson, F.M., Kinsey, B., Kosten, T., & Brimijoin, S. The concept of pharmacologic cocaine interception as a treatment for drug abuse. *Chemico-Biological Interactions*, 2010.

[103] Colfax, G. & Guzman, R. Club drugs and HIV infection: A review. *Clinical Infectious Diseases* 42, 1463–1469, 2006.

[104] Hagan, H., Campbell, J., Thiede, H., Strathdee, S., Ouellet, L., Kapadia, F., Hudson, S., & Garfein, R.S. Self-reported hepatitis C virus antibody status and risk behavior in young injectors. *Public Health Reports* 121, 710–719, 2006.

[105] Amon, J.J., Garfein, R.S., Ahdieh-Grant, L., Armstrong, G.L., Ouellet, L.J., Latka, M.H., Vlahov, D., Strathdee, S.A., Hudson, S.M., Kerndt, P., Des Jarlais, D., & Williams, I.T. Prevalence of hepatitis C virus infection among injection drug users in the United States, 1994–2004. *Clinical Infectious Diseases* 46, 1852–1858, 2008.

[106] Schiavini, M., Angeli, E., Mainini, A., Zerbi, P., Duca, P.G., Gubertini, G, Vago, L., Fociani, P., Giorgi, R., & Cargnel, A. Risk factors for fibrosis progression in HIV/HCV coinfected patients from a retrospective analysis of liver biopsies in 1985–2002. *HIV Medicine* 7, 331–337, 2006.

[107] Institute of Medicine. *Hepatitis and Liver Cancer: A National Strategy for Prevention and Control of Hepatitis B and C*. Washington, DC: National Academies Press, 2010.

[108] Soriano, V., Vispo, E., Labarga, P., Medrano, J., & Barreiro, P. Viral hepatitis and HIV co-infection. *Antiviral Research* 85, 303–315, 2010.

[109] Mehta, S.H., Genberg, B.L., Astemborski, J., Kavasery, R., Kirk, G.D., Vlahov, D., Strathdee, S.A., & Thomas, D.L. Limited uptake of hepatitis C treatment among injection drug users. *Journal of Community Health* 33, 126–133, 2008.

[110] Mehta, S.H., Thomas, D.L., Sulkowski, M.S., Safaein, M., Vlahov, D., & Strathdee, S.A. A framework for understanding factors that affect access and utilization of treatment for hepatitis C virus infection among HCV-mono-infected and HIV/HCV-co-infected injection drug users. *AIDS* 19 Suppl 3, S179–189, 2005.

[111] World Health Organization (WHO). WHO Global tuberculosis control - surveillance, planning, financing. In *WHO Report*. Geneva, 2006.

[112] Oeltmann, J.E., Kammerer, J.S., Pevzner, E.S., & Moonan, P.K. Tuberculosis and substance abuse in the United States, 1997–2006. *Archives of Internal Medicine* 169, 189–197, 2009.

[113] Reported HIV Status of Tuberculosis Patients—United States, 1993–2005. *MMWR* 56, 1103–1106, 2007.

[114] Rehm, J., Samokhvalov, A.V., Neuman, M.G., Room, R., Parry, C., Lonnroth, K., Patra, J., Poznyak, V., & Popova, S. The association between alcohol use, alcohol use disorders and tuberculosis (TB). A systematic review. *BMC Public Health* 9, 450, 2009.

[115] Tsiouris, S.J., Gandhi, N.R., El-Sadr, W.M., & Gerald, F. Tuberculosis and HIV-Needed: A New Paradigm for the Control and Management of Linked Epidemics. *Journal of the International AIDS Society* 9, 62, 2007.

[116] Bruce, R., Altice, F. & Friedland, G. HIV Disease Among Substance Misusers: Treatment Issues. In *Global AIDS/HIV Medicine* (ed. Volberding, P.A.). San Diego, CA: Elsevier, Inc, 2007.

[117] Kreek, M.J., Garfield, J.W., Gutjahr, C.L., & Giusti, L.M. Rifampin-induced methadone withdrawal. *New England Journal of Medicine* 294, 1104–1106, 1976.

[118] Bruce, R.D. & Altice, F.L. Clinical care of the HIV-infected drug user. *Infectious Disease Clinics of North America* 21, 149–179, ix, 2007.

[119] Bruce, R.D., McCance-Katz, E., Kharasch, E.D., Moody, D.E., & Morse, G.D. Pharmacokinetic interactions between buprenorphine and antiretroviral medications. *Clinical Infectious Diseases* 43 (Suppl 4), S216–223, 2006.

[120] McCance-Katz, E.F., Moody, D.E., Morse, G.D., Friedland, G., Pade, P., Baker, J., Alvanzo, A., Smith, P., Ogundele, A., Jatlow, P., & Rainey, P.M. Interactions between buprenorphine and antiretrovirals. I. The nonnucleoside reverse-transcriptase inhibitors efavirenz and delavirdine. *Clinical Infectious Diseases* 43 (Suppl 4), S224–234, 2006.

[121] McCance-Katz, E.F., Moody, D.E., Morse, G.D., Ma, Q., DiFrancesco, R., Friedland, G., Pade, P., & Rainey, P.M. Interaction between buprenorphine and atazanavir or atazanavir/ritonavir. *Drug and Alcohol Dependence* 91, 269–278, 2007.

[122] McCance-Katz, E.F., Moody, D.E., Smith, P.F., Morse, G.D., Friedland, G., Pade, P., Baker, J. Alvanzo, A., Jatlow, P., & Rainey, P. M. Interactions between buprenorphine and antiretrovirals. II. The protease inhibitors nelfinavir, lopinavir/ritonavir, and ritonavir. *Clinical Infectious Diseases* 43 (Suppl 4), S235–246, 2006.

[123] DeBeck, K., Kerr, T., Li, K., Fischer, B., Buxton, J., Montaner, J., & Wood, E. Smoking of crack cocaine as a risk factor for HIV infection among people who use injection drugs. *Canadian Medical Association Journal* 181, 585–589, 2009.

[124] Farrell, M., Marsden, J., Ali, R., & Ling, W. Methamphetamine: Drug use and psychoses becomes a major public health issue in the Asia Pacific region. *Addiction* 97, 771–772, 2002.

[125] Fairbairn, N., Kerr, T., Buxton, J.A., Li, K., Montaner, J.S., & Wood, E. Increasing use and associated harms of crystal methamphetamine injection in a Canadian setting. *Drug and Alcohol Dependence* 88, 313–316, 2007.

[126] Nacher, M., Adenis, A., Adriouch, L., Vantilcke, V., El Guedj, M., Vaz, T., Dufour, J., & Couppie, P. Crack cocaine use increases the incidence of AIDS-defining events in French Guiana. *AIDS* 23, 2223–2226, 2009.

[127] Santibanez, S.S., Garfein, R.S., Swartzendruber, A., Kerndt, P.R., Morse, E., Ompad, D., Strathdee, S., Williams, I.T., Friedman, S.R., & Ouellet, L.J. Prevalence and correlates of crack-cocaine injection among young injection drug users in the United States, 1997–1999. *Drug and Alcohol Dependence* 77, 227–233, 2005.

[128] Leukefeld, C.G., Pechansky, F., Martin, S.S., Surratt, H.L., Inciardi, J.A., Kessler, F.H., Orsi, M.M., Von Diemen, L., & Meyer Da Silva, E. Tailoring an HIV-prevention intervention for cocaine injectors and crack users in Porto Alegre, Brazil. *AIDS Care* 17 (Suppl 1), S77–87, 2005.

[129] Rawson, R.A., McCann, M.J., Flammino, F., Shoptaw, S., Miotto, K., Reiber, C., & Ling, W. A comparison of contingency management and cognitive-behavioral approaches for stimulant-dependent individuals. *Addiction* 101, 267–274, 2006.

[130] Aidala, A., Cross, J.E., Stall, R., Harre, D., & Sumartojo, E. Housing status and HIV risk behaviors: Implications for prevention and policy. *AIDS and Behavior* 9, 251–265, 2005.

[131] Kidder, D.P., Wolitski, R.J., Royal, S., Aidala, A., Courtenay-Quirk, C., Holtgrave, D.R., Harre, D., Sumartojo, E., Stall, R., & the Housing and Health Study Team. Access to housing as a structural intervention for homeless and unstably housed people living with HIV: Rationale, methods, and implementation of the housing and health study. *AIDS and Behavior* 11, S149–S161, 2007.

[132] Briggs, D., Rhodes, T., Marks, D., Kimber, J., Holloway, G., & Jones, S. Injecting drug use and unstable housing: Scope for structural interventions in harm reduction. *Drugs: Education Prevention and Policy* 16, 436–450, 2009.

[133] Blankenship, K.M., Friedman, S.R., Dworkin, S., & Mantell, J.E. Structural interventions: Concepts, challenges and opportunities for research. *Journal of Urban Health* 83, 59–72, 2006.

[134] Mathers, B.M., Degenhardt, L., Adam, P., Toskin, I., Nashkhoev, M., Lyerla, R., & Rugg, D. Estimating the level of HIV prevention coverage, knowledge and protective behavior among injecting drug users: What does the 2008 UNGASS reporting round tell us? *Journal of Acquired Immune Deficiency Syndromes* 52, S132–142, 2009.

Chapter 4. Expanded HAART to Improve Individual and Public Health Outcomes

Remarkable advances in HIV therapeutics have taken place over the last two decades.[1] Highly active antiretroviral therapy (HAART) is the most significant development.[2] HAART refers to a combination of antiretroviral drugs, typically three, that can fully suppress HIV replication. With the use of HAART, the number of plasma HIV-1-RNA viral copies rapidly becomes undetectable, as measured by the most sensitive commercially available assays. This allows for immune reconstitution to take place, arresting the otherwise fatal course of the disease and putting HIV infection into remission on a long-term basis.[3]

Dramatic reductions in morbidity and mortality in HIV-infected patients have been shown in clinical trials and observational studies evaluating the efficacy of HAART.[4-5] By 2006, it was estimated that at least 3 million years of life had been saved in the United States as a direct result of the rollout.[6] It has also been estimated that the average number of years remaining to live among HIV-infected individuals on HAART at age 20 in high-income countries is about two-thirds of that of the general population.[7]

Recent World Health Organization (WHO) estimates suggest that more than 4 million people were receiving HAART in low- and middle-income countries at the end of 2008.[8] This falls short of the original 2006 United Nations (UN) commitment to achieving "universal access to HIV prevention, treatment, care, and support by 2010." Despite this limitation, the rollout of HAART has undoubtedly had a major impact on HIV/AIDS morbidity and mortality in resource-limited settings around the world.[9-11]

Seek, Test, Treat, and Retain

This section will present the new paradigm of expanding HAART coverage as a tool in the armamentarium of HIV prevention. This new paradigm can be characterized as seek, test, treat, and retain, where the components are as follows: seek is outreach to high-risk, hard-to-reach populations, test is HIV testing; treat is linkage to HIV treatment and other services; and retain is maintaining and sustaining individuals in care. This paradigm was referred to as "seek, test, and treat" at the outset of the 2010 consultation meeting, but it was the consensus of the group to add "retain" to highlight the critical importance of retention in treatment. Issues relating to the implementation of seek, test, treat, and retain in drug-using populations are addressed below.

> "The HIV field has a moral and ethical obligation to acknowledge that HAART works among drug- using populations, and therefore could do a much better job of controlling HIV in this community if antiretroviral therapy was more aggressively deployed as part of a combination prevention package."
>
> Julio Montaner, M.D.,
> President,
> International AIDS Society

HAART has been associated with dramatic decreases in AIDS-related morbidity and mortality in resource-rich as well as resource-limited areas of the world. These benefits can be demonstrated regardless of the mode of acquisition of HIV infection. More recently, a secondary benefit of HAART has been demonstrated in its ability to decrease HIV transmission.[12-14] HAART as an important component of HIV prevention interventions is receiving increased attention.[15]

The immediate implementation of an aggressive strategy aimed at rapidly expanding antiretroviral therapy (ART) to all those in medical need, based on current medical guidelines, is fully warranted.[16] The imperative to roll out this strategy is based on the proven, patient-centered benefits of HAART in decreasing AIDS-related morbidity and mortality, which alone render this approach highly cost-effective.[17] Implementation of this strategy cannot wait for the actual impact of HAART on HIV transmission to be fully characterized, even though it might vary widely among populations and settings.[18-19] Recent findings on the direct and multiple secondary benefits of the expansion of HAART coverage

serve as a powerful impetus for an aggressive global rollout of HAART.[20]

The expansion of HAART should be carried out within a comprehensive "combination prevention" framework.[7,21] Additionally, coverage expansion should include enhanced case finding, as well as supportive and culturally sensitive strategies to promote, facilitate, and support engagement and maintenance in care, particularly among hard-to-reach populations.[22] The rapid expansion of antiretroviral therapy coverage also should be implemented with full consideration of human rights, including the need to respect patients' privacy and autonomy.[23] Evaluation of the potential impacts of seek, test, treat, and retain outside the areas in which HAART treatment is medically indicated is critical.[24-25] Current treatment guidelines leave relatively few outside of the "treatment envelope," making it difficult, if not futile, to pursue traditional, randomized clinical trial approaches to evaluate the intervention on a long-term basis.[26-28] Other approaches, such as a "delayed start" design, may be more appropriate.[29] This strategy could accelerate and address the impact of effective rollout of HAART in diverse settings and populations. Close prospective monitoring of such initiatives, implemented in a variety of settings and populations, will provide invaluable lessons in optimizing outcomes.

> "All scientific work is incomplete—whether it be observational or experimental. All scientific work is liable to be upset or modified by advancing knowledge. That does not confer upon us freedom to ignore the knowledge we already have or to postpone the action that it appears to demand at a given time".[30]
>
> Sir Austin Bradford-Hill

Treatment as Prevention

A rapidly growing body of evidence indicates that the expansion of HAART coverage can help reduce the transmission of HIV.[18,31-36] HAART rapidly and effectively suppresses viral replication, rendering the plasma HIV-1-RNA viral load undetectable on a sustained basis. As a result, HAART also decreases HIV-1-RNA viral load in other biological fluids, including semen and vaginal secretions.[7,37-38] Exceptions to the correlation between plasma viral load and other biological fluids have been reported, which is particularly relevant to counseling on safe sex and other harm reduction practices.[39] However, from a public health perspective, the correlation between HAART and HIV-1-RNA viral load levels in plasma and other bodily fluids is quite strong, particularly in the case of long-term, sustained, and effective HAART.

Strong proof of principle regarding the impact of HAART on HIV transmission can be found in studies of vertical transmission.[40] In this setting, HIV transmission has been virtually eliminated when HAART is used appropriately. As a result, there has been a call for worldwide expansion of HAART programs to eliminate neonatal HIV globally.[41]

The preventive role of HAART in HIV serodiscordant heterosexual couples has now been documented in a number of observational studies. Attia et al. completed a meta-analysis involving over 1,000 person-years from five cohorts of heterosexual HIV serodiscordant couples.[13] No events of HIV transmission were documented when the index patient was receiving antiretroviral therapy and had a plasma HIV-1-RNA viral load below 400 copies/mL. When the confidence intervals around the estimate are considered, the data were compatible with one transmission per 79 person-years. Further precise, quantitative evidence about the effect of HAART on HIV transmission is expected to emerge from HPTN 052—an ongoing randomized controlled trial of treatment as prevention involving more than 1,700 serodiscordant heterosexual couples—currently underway under the auspices of the National Institutes of Health (NIH).[42]

At the population level, the effect of the initial rollout of HAART in 1996 on HIV transmission in Taiwan and British Columbia has been documented. The initial rollout of HAART in Taiwan was associated with a 53% reduction in new HIV-positive diagnoses between 1996 and 1999.[43] In British Columbia, Canada, new yearly HIV infections decreased by approximately 50% over the same time frame, coinciding with the introduction of HAART.[33] The similar reductions in HIV diagnoses in Taiwan and British Columbia occurred in the context of differing rates of syphilis, a marker of high-risk sexual behavior in the community. In Taiwan, syphilis rates were stable, while in British Columbia, rates increased steadily over the study period.[33,43]

Based on the British Columbia experience, Lima et al. estimated the potential decrease of HIV incidence that would be associated with a stepwise increase in HAART coverage.[44] The model also considered HIV drug resistance resulting from changes in adherence, because increased coverage engages harder-to-reach populations that may have adherence challenges. Overall, the model suggested that increased HAART coverage will lead to proportional decreases in HIV transmission that are not likely to be overwhelmed by decreasing

adherence or increasing resistance rates. Of note, the latter is at least partially attributable to the fact that a relatively high level of adherence is required to select for and maintain resistant viral strains. Very low levels of adherence or nonadherence invariably allow the original viral strains, typically wild-type virus, to overwhelm the resistant virus.[45] Separately, drug-resistant HIV is characterized by decreased fitness, which is most often associated with decreased plasma HIV-1-RNA viral load, an important determinant of decreased HIV transmission.[46]

Antiretroviral –naïve subjects with and without a history of injection drug use followed for 30 months after initiating HAART have been shown to have similar rates of drug resistance.[47] A recent population-level study of patients in British Columbia who initiated antiviral therapy between 1996 and 2008 demonstrated dramatic decreases in the incidence of antiviral drug resistance concomitant with increases in exposure to antiretroviral drugs and increases in the proportion of patients achieving viral suppression.[48]

HAART Use Among HIV-Infected Drug Users

The use of HAART among HIV-infected drug users has been a subject of considerable debate in the literature. A number of reports have argued that social instability related to illicit drug use can compromise HAART-related benefits.[49-51] As a result, drug users have been less likely to be prescribed HAART.[52-53]

The effectiveness of HAART in a drug-using population was recently tested. In a population-based cohort study of more than 3,000 antiretroviral-naive HIV-infected patients to compare HAART's outcomes between individuals with and without a history of injection drug use.[54] A total of 915 participants were injection drug users. Median duration of follow-up was over 5 years. Overall, at 84 months after the initiation of HAART, rates of death were statistically not significantly different between the two groups; the hazard ratio of mortality was 1.09 (95% CI, 0.92-1.29). Similar results were found when the analysis was restricted to nonaccidental deaths. These results suggest that HAART has a similar survival benefit at the population level between individuals with and without a history of injection drug use.

More recently, potential secondary benefit of HAART on HIV transmission among injection drug users was evaluated.[14] Given that needle sharing is an important determinant of HIV transmission, and given that this is not a behavior typically restricted to a single or even a limited number of partners, researchers approached this issue by examining HIV transmission and HAART use at the community level. This was done using two preexisting research cohorts in the downtown eastside (DTES) of Vancouver. The DTES represents the poorest neighborhood in Canada. This small geographical area has a large number of drug users and a particularly high prevalence of intravenous drug use. A number of prospective cohorts were established in the mid-1990s in the DTES to evaluate the outcomes of HIV infection among those already infected and the risk factors related to acquisition of HIV infection among those not yet infected. The research team was therefore able to estimate at semiannual intervals the "community plasma-HIV-1-RNA level" within the cohort of HIV-positive individuals and the HIV seroconversion rate in the HIV-negative injection drug-using cohort.

In a multivariate model that adjusted for sharing of used syringes, unprotected sex, ethnicity, daily cocaine use, daily heroin use, and unstable housing, the median "community plasma HIV-1-RNA level" remained independently associated with the time to HIV seroconversion, with a hazard ratio of 3.32 (1.82 to 6.08, $p < 0.001$) per log10 increase in plasma HIV-1-RNA viral load. The driver of the observed reduction in the community plasma HIV-1-RNA levels over time in this cohort was the use of HAART, which increased from 8% in 1996 to 99% in 2007. These results show for the first time that a longitudinal measure of "community plasma HIV-1-RNA level" correlates with the HIV incidence rate in the community and can predict HIV incidence independent of unsafe sexual behaviors and syringe sharing in the setting of injection drug use. These results provide a strong rationale for reexamining the HIV prevention and treatment dichotomy, as well as the need for aggressive expansion of HAART among HIV-infected drug users.

Missed Opportunities for Seek, Test, Treat, and Retain Among Drug-Using Populations

Drug use has played a major role in HIV transmission. While a number of interventions have been successful in curbing HIV transmission among people who inject drugs, more attention is urgently needed to address HIV transmission among noninjection drug users. An aggressive approach to HIV prevention and treatment is needed to reverse current trends observed across drug-using populations globally. Questions that address why drug users haven't been tested or treated for HIV are very important, as the field is seeking the optimal way to test and treat. As described previously, the "seek, test, treat, and retain" model involves reaching out to high-risk, hard-to-reach groups who have not been recently

tested (seek); engaging them in HIV testing (test); and initiating, monitoring, and maintaining HAART for those testing positive (treat); and retaining them in treatment (retain).

At the consultation meeting, Dr. Nora Volkow, Director of NIDA, discussed the missed opportunities of engaging substance abusers in HIV testing at substance abuse treatment centers. Dr. Volkow noted that less than one-third of U.S. drug treatment programs[55] and only one-half of NIDA Clinical Trials Network (CTN) treatment programs offer HIV testing and counseling.[56] She also presented data from the Centers for Disease Control and Prevention (CDC) indicating that of persons 18 to 64 who reported being tested for HIV in 2006, only 0.4% reported being tested in a drug treatment facility.[57]

To better understand the parameters affecting acceptance of HIV testing at substance abuse treatment centers, the NIDA CTN recently completed a study, CTN 0032, HIV Rapid Testing and Counseling, led by Drs. Metsch and Colfax. The study was conducted in 12 drug treatment sites across the country. It had three arms: (1) on-site HIV rapid testing with brief, participant-tailored prevention counseling; (2) on-site rapid testing with information only; and (3) referral off-site for testing. When data from this study are fully analyzed, they should provide information on the relative effectiveness of these three testing strategies in ensuring that persons in drug treatment programs are tested for HIV, receive their test results, and decrease HIV sexual risk behaviors. Dr. Volkow presented some of the early findings from this study. The total number of patients screened was 2,452, with the following demographics: 41.3% female, 10.4% Hispanic, 27.2% Black, and 59.7% White; and 46.3% were injection drug users. Twenty-eight percent had been HIV-tested in the past year; 52% had been tested more than a year previously; and 20% had never been tested. (The CDC recommends annual testing for those in vulnerable populations.) The study found that 96.4% tested HIV negative and 3.6% were found to be HIV positive. Based on pre- and post-randomization information, an estimated 70% to 80% would accept being HIV-tested. The main reasons cited for not being tested previously were, "have not found the place to do the testing" and "denial of risk."

HIV Testing by Gender

N=2452

$\chi_{(2)}$=75.79 p<.0001	In Last Yr	>Yr Ago	Never
Females	30.6%	57.6%	**11.9%**
Males	25.5%	48.3%	**26.2%**

HIV Testing by Race/Ethnicity

N=2385

$\chi_{(2)}$=75.79 p<.0001	In Last Yr	>Yr Ago	Never
Hispanic	**22.3%**	57.4%	**20.3%**
Black	**41.4%**	47.2%	**11.7%**
White*	**22.2%**	53.3%	**24.5%**

*Non-Hispanic; note Other Category not shown

Dr. Volkow also identified key challenges in HIV treatment among the drug-using populations, including:

- HIV treatment adherence is poor without proper treatment for addiction;
- Late testing is a problem (i.e., the disease has progressed, so the mortality rate is high); and
- Many HIV-positive drug users have comorbidities (i.e., co-infections and mental health problems).

HIV/AIDS Treatment for Drug-Using Populations

Dr. Roy M. Gulick of Weill Cornell Medical College presented on the use of ART in HIV/AIDS treatment. He noted that antiretroviral therapy changes the natural history of HIV infection by preventing clinical progression.[58-59] With the development of effective combination antiretroviral therapy in the mid-1990s and rapid widespread clinical use in developed countries, deaths in individuals with HIV/AIDS dropped by two-thirds from 1995 to 1997. Since the late 1990s, ART regimens became easier to take, less toxic, and more potent. Today, an effective ART regimen can be as simple as one pill at bedtime. ART use in developing countries expanded markedly after 2000, and an estimated 4 million HIV-infected people in developing countries are taking ART today, with demonstrated clinical benefits similar to those seen in developed countries.

Despite these marked improvements, Dr. Gulick stated that challenges of access, adherence, toxicity, and drug resistance remain, particularly among disadvantaged populations. Some

groups have lagged in benefiting from ART. They include injection drug users who have lower life expectancy due to a number of factors, including access, adherence, and concomitant conditions (including mental health disorders and HCV infection). [59] Despite more than 20 years of ART, basic clinical questions continue to be posed: When to start ART? What regimen to start? When to change an ART regimen? What ART regimen to change to?

When to Start ART?

Dr. Gulick stated that the optimal time to start ART in an HIV-infected individual remains unknown.[27,60-63] Concerning when to start antiretroviral therapy: The rationale for starting ART early includes the facts that HIV disease is progressive, ART decreases HIV RNA (viral load) levels and the risk of the emergence of drug resistance, and increases CD4 cell counts and general immune function that delay or prevent clinical complications (both HIV-related and other). In addition, ART regimens are durable, and ART likely decreases HIV transmission in the community. The rationale for delaying ART includes practical factors, such as the requirement for long-term adherence; and the fact that drug toxicities may occur, long-term side effects of ART are unknown, and the risk of clinical events is low in earlier HIV disease.

The current standard of care worldwide is to start ART for symptomatic HIV disease and/or a CD4 cell count of less than 350/uL.

Guidelines for Initiation of ART

	AIDS/Sx	CD4 <200	CD4 200-350	CD4 350-500	CD4 >500
DHHS '09 www.aidsinfo.nih.gov	YES	YES	YES	**YES**	**YES (optional)**
IAS-USA '08 Hammer JAMA 2008, 300:555	YES	YES	YES	individualize	individualize
UK '08 www.bhiva.org	YES (except TB)	YES	YES	clinical trial	clinical trial
EACS '09 www.eacs.eu	YES	YES	YES	**certain pts.**	**defer**
WHO '09 www.who.int/hiv/pub/guidelines/adult/en/	YES	YES	**YES**	NO	NO

Developed world guidelines also note clinical scenarios in which ART should be started in certain patients with CD4 cell counts >350/uL, including: hepatitis B virus infection requiring treatment, HIV-associated nephropathy, pregnancy, and hepatitis C virus co-infection.[60-61] The European Guidelines also suggest considering the initiation of ART in patients with CD4 cell counts >350/uL who are more than 50 years old, or who have CD4 cell counts declining more than 50-100 cells/uL per year, HIV RNA levels >100,000 copies/ml, high risk of cardiovascular disease, and/or malignancy.[61] On the basis of improved ART and emerging data about increased non–HIV-related clinical events from cohort studies, the U.S. Department of Health and Human Services (DHHS) ART Guidelines recently changed their recommendations to starting ART earlier.[62] These guidelines now recommend ART for patients with CD4 cell counts 350-500/uL). In addition, the guidelines now also support ART for patients with CD4 cell counts >500/uL. The recent WHO Guidelines specifically do NOT support starting ART in patients with CD4 cell counts >350/uL. All ART guidelines agree that patient readiness is a key factor in deciding the optimal time to start ART.

What ART to Start?

Dr. Gulick explained that ART drugs fall into six distinct classes based on their mechanism of action. The first class of antiretroviral drugs approved was the HIV nucleoside-analogue reverse transcriptase inhibitors (NRTI) in 1987.[64] By the mid-1990s, two additional classes were approved: the HIV non-nucleoside reverse transcriptase inhibitors (NNRTI)[65-66] and the HIV protease inhibitors (PI).[67-69] It was not until 2003 that the fourth class of drugs was approved: the first HIV fusion inhibitor.[70-71] In 2007, two additional classes were approved: the first CCR5 chemokine receptor antagonist[72-73] and the first HIV integrase inhibitor.[74-75] In addition to the development of these new classes of drugs, improved formulations of antiretroviral drugs have become available, including co-formulations of two or three antiretroviral drugs into a single pill to improve adherence.

For initial treatment of HIV infection, current ART guidelines worldwide recommend a combination regimen consisting of three antiretroviral drugs, most commonly two nucleoside-analogue reverse transcriptase inhibitors, together with a non-nucleoside reverse transcriptase inhibitor.[27,60-63] U.S. Guidelines additionally recommend two nucleoside-analogue reverse transcriptase inhibitors, together with an HIV protease inhibitor.[62] These regimens demonstrate potent, durable virologic suppression and enhancement of CD4 cell counts and general immune function. Guidelines recommend certain drugs within a class as preferred, alternate, or acceptable choices, based on their efficacy, convenience, toxicity, drug resistance profile, and other factors.

Current U.S. DHHS ART Guidelines recommend as preferred therapy for initial treatment of HIV infection the nucleoside-analogue combination of tenofovir/emtricitabine (co-formulated), together with either the NNRTI, efavirenz (co-formulated with tenofovir/emtricitabine as a three-drug regimen that can be given as one pill, once-daily); a protease inhibitor (PI), either atazanavir or darunavir (each given together with low-dose ritonavir to enhance drug levels); or the integrase inhibitor, raltegravir.[62]

Current WHO Guidelines recommend as preferred therapy for initial treatment of HIV infection the dual nucleoside-analogue combinations of either tenofovir + emtricitabine, tenofovir + lamivudine, or zidovudine + lamivudine, in combination with an NNRTI, either efavirenz or nevirapine.[63] These guidelines are based not only on considerations for efficacy, convenience, toxicity and drug resistance, but also access, availability (including generic formulations), and cost. An NRTI that was recommended in prior guidelines, stavudine (d4T), is no longer recommended because of toxicities, including peripheral neuropathy, facial lipoatrophy, and lactic acidosis.

Choosing among these initial drug options requires consideration of a number of individual patient factors, such as the following: preexisting drug-resistant virus, tolerability (both acute and chronic), adherence, convenience (e.g., number of pills, dosing interval, food/fasting requirements), stage of HIV disease, concomitant illnesses (e.g., psychiatric illness, substance use, viral hepatitis), drug–drug interactions with other medications, preserving future treatment options, access, and cost. The optimal antiretroviral drug regimen is one that has been individualized for a particular patient.

When to Switch ART?

While most patients will succeed on ART, some will experience regimen failure, requiring ART to be changed. The initial approach to treatment failure is to identify the reason(s) for failure and try to address these better in the selection of the subsequent ART regimen.

The U.S. DHHS ART Guidelines outline specific clinical scenarios that define treatment failure:

- Virologic failure can be defined as an incomplete virologic response, e.g., HIV RNA >400 copies/ml by 24 weeks or >50 copies/ml by 48 weeks, or virologic rebound (i.e., after prior virologic suppression, confirmed recurrent detectable viral load level).[62] Continuing ART in the setting of ongoing virologic suppression over time leads to the emergence of viral variants with mutations that confer drug resistance to the drugs in the regimen. Because of cross-resistance, these resistant viral variants often are also resistant to other drugs in the same mechanistic class. Virologic failure is the most common form of treatment failure and should be addressed and treated aggressively by changing treatment.
- Immunologic failure can be defined as a failure to achieve and maintain an adequate CD4 cell response (despite virologic suppression) and occurs in approximately 10-15% of patients.[62] While some causes of immunologic failure can be identified and addressed (e.g., drug-induced leukopenia), many patients have immunologic failure of unknown cause and there are few, if any, available treatment options other than simply continuing virologically suppressive ART.
- Finally, clinical failure can be defined as the occurrence or recurrence of HIV-related clinical events. In assessing for clinical failure, it is important to exclude an immune reconstitution syndrome (IRIS), an inflammatory response that typically is induced within the first 3 months after starting an effective ART regimen. Treatment of IRIS (if necessary) usually consists of anti-inflammatories (non-steroidal or steroids); ART most often is continued in this setting.[76]

In settings of limited resources, WHO Guidelines define treatment failure differently:

- Virologic failure is defined as a persistent HIV RNA level above 5000 copies/ml. The guidelines recommend using HIV RNA to confirm treatment failure (when available) every 6 months. When HIV RNA testing is not available, the guidelines use immunological criteria to confirm treatment failure. Previous studies showed that clinical monitoring alone (i.e., changing ART following an AIDS-related illness) resulted in increased mortality and disease progression compared to combined immunological and clinical monitoring[77] or combined virological, immunological, and clinical monitoring.[78] One concern for setting a higher HIV RNA threshold for virologic failure (>5000 copies/ml) is the selection of drug-resistant viral strains.

While the WHO Guidelines stress that unnecessary switching to expensive second-line therapy should be avoided, the issue of selection of drug-resistant viral strains remains an important consideration in optimal ART management.

What ART Drugs to Switch to?

Dr. Gulick addressed the DHHS Guidelines as an approach to selecting a subsequent ART regimen.[62] First, the goals of therapy should be reviewed. The current goal for all HIV-infected individuals treated with ART, regardless of prior treatment, is maximal virologic suppression (e.g., HIV RNA <50 copies/ml). However, for some patients with extensive prior treatment and no treatment options, a reasonable treatment goal is to preserve immune function and avoid clinical progression. The ART history should be reviewed and adherence and tolerability of prior ART regimens assessed. Concomitant medications and the potential for drug–drug interactions with antiretroviral drugs should be considered. Drug resistance testing should be performed while the patient is taking the antiretroviral regimen (or within 4 weeks of discontinuation). For first- or second-line therapy, genotypic drug resistance testing is recommended; for subsequent regimen failures, both genotypic and phenotypic drug resistance testing is recommended. From the history and drug resistance testing results, the goal is to identify susceptible drugs and drug classes and consider using newer agents, including those available through expanded access or clinical trials. The ultimate goal is to design a new regimen with two (or preferably three) fully active agents. This strategy offers the best chance of reestablishing virologic control.

The WHO Guidelines for resource-limited settings focus on choices for second-line ART, following failure of first-line ART. They recommend using a ritonavir-boosted protease inhibitor (either atazanavir or lopinavir) with two nucleoside analogues. For the choice of NRTIs, they recommend: if d4T or ZDV was used first-line, use TDF (with 3TC or FTC) second-line; and if TDF was used first-line, use ZDV + 3TC in second-line. Some of the newer drugs are becoming available in resource-limited settings, including darunavir and raltegravir.

What Are the Next Steps in ART Research?

The question of the optimal time to begin ART currently is being addressed in a large, ongoing clinical trial called the START study that seeks to enroll more than 4,000 treatment-naïve patients with CD4 counts >500 cells/uL, randomizing them to start ART immediately or to delay until the CD4 count is <350 cells/uL. A number of additional comparative studies comparing initial ART regimens head to head are in progress, including some with investigational agents. Newer and novel formulations of ART may allow less frequent dosing (e.g., once a week, twice a month, once a month); clinical studies are planned.

> "Medications do not work in patients who do not take them."
>
> C. Everett Koop, M.D.,
> former U.S. Surgeon General

Adherence to ART Among Drug-Using Populations

Dr. Robert Gross, University of Pennsylvania School of Medicine, addressed adherence to antiretroviral therapy at the consultation meeting, as adherence is a priority issue among HIV-infected, drug-using populations. He stated that active drug users are at increased risk of ongoing HIV-transmitting behaviors (including continued sharing of injection equipment and sex with multiple partners in exchange for drugs or money). Nonadherence to both HIV treatment and HIV prevention practices increases the risk of HIV transmission from HIV-infected drug users. Moreover, because partial adherence leads to the emergence of HIV that is resistant to the regimen, active drug users also are at increased risk of harboring and thereby transmitting resistant virus.

To date, no predictive model for adherence among people who use drugs exists. While past adherence is associated with future adherence, individuals can improve or worsen with adherence over time. Given the lifesaving nature of antiretroviral therapy, it is ill-advised to withhold antiretroviral therapy in anticipation of nonadherence. Rather, creating an environment that maximizes the substance abuser's ability to adhere is preferred. This section will address several facets of the issue of adherence among drug-using populations, including the relationship between adherence and treatment outcomes, methods for measuring adherence, barriers to adherence, and interventions to improve adherence.

Adherence and Treatment Outcomes

Over the past 15 years, numerous studies using various methods for measuring adherence have demonstrated the relationship between adherence and treatment outcomes.[79-83] In most studies, when more than 80% of doses are taken, more than half of individuals achieve treatment success. When 95% of doses are taken, the vast majority of individuals (i.e., more than 8 out of 10) achieve treatment success.

Dr. Gross said adherence to antiretroviral therapy is particularly important because the consequences of treatment failure are dramatic (i.e., continued viral replication, emergence of

resistance, and death). The strength of the relation between adherence and survival is less stark; the proportion of individuals surviving at lower levels of adherence is higher than the proportion of individuals with virological success at that same level.[54,80,84-85] Therefore, antiretroviral therapy is lifesaving even at suboptimal levels of adherence. The reasons for this observation are not fully explained, but they may relate to the decreased immunopathogenesis of partially suppressed and/or resistant virus.

The relationship between adherence and the emergence of resistant virus in the individual is less well understood and likely varies by drug-resistance mechanism, pharmacokinetics, and pharmacodynamics.[7,86-87] For some drugs, the highest risk for resistance occurs at very high levels of adherence, while for others, moderate levels of adherence confer the greatest risk.[88] And as seen in maternal-to-child transmission studies, even a single dose of antiretrovirals with no further drug exposure (akin to near total nonadherence) results in higher rates of treatment failure.[89] Given the complexity of these relationships, the lack of a threshold that clearly decreases the risk of resistance, the survival benefit that continues to accrue as adherence levels increase, and the inability to predict treatment response in the individual, patients are encouraged to adhere to the highest degree possible.

Measurement of Adherence

According to Dr. Gross, a variety of methods to measure adherence are available, all of which have strengths and limitations. Self-reports can be performed by staff or by computerized self-interview.[90] The strength is convenience when direct patient contact occurs. The weakness is the need to ask questions in a nonjudgmental manner/atmosphere, which is not always possible in the clinical setting. Also, assessments of periods of time longer than a few days, for detailed information, or a month, for most general data, are unlikely to be accurate. Further, self-reports are susceptible to underreporting of nonadherence, either due to forgetting that doses were missed or intentional deception.[91]

The strength of pharmacy refill data is that these data are more objective in nature, they often are captured in routine clinical care, and they have the ability to capture adherence data over long periods of time.[92-93] Disadvantages include lack of validity when refills are automatic and perhaps when refills are required to coincide with clinic visits. Microelectronic monitors are thought to be the most accurate measures of adherence, but they are too expensive for clinical practice in almost all settings and often are inconvenient because they require the medication to be packaged with the device (often precluding interventions such as pill organizers).[94] Other techniques that are less often used, but valid in certain settings, include drug concentrations in plasma and hair.[95-96]

As with substance abuse, adherence is a time-varying behavior.[97] An individual who is adherent now may be nonadherent later, and vice-versa. In fact, many studies have demonstrated that adherence tends to wane over time in a large proportion of the initially adherent population. Thus, it is particularly important to measure adherence at intervals and not assume that once high levels of adherence are achieved, they will be maintained. Therefore, whichever adherence technique is used, adherence must be re-measured at intervals to capture the adherence period of particular interest.

The frequency of measuring adherence depends on the goal of measurement and the method used. Typically, the goal of measuring adherence in the clinical setting is to determine whether further adherence intervention is needed. Although adherence takes place along a continuum and the relationship between nonadherence and treatment failure likely varies by individual and regimen, the sooner one intervenes in recognized nonadherence, the more likely the intervention is to forestall treatment failure. The duration of this window of opportunity during which nonadherence begins and treatment failure becomes irrevocable has not been fully explored, but it is thought to be on the order of weeks to months.[98]

If the earliest sign of any missed doses is desired for interventions to be implemented, shorter intervals are preferred. However, this must be balanced by the fact that an individual missing one dose might be labeled as nonadherent. Yet, a single dose missed may not be a harbinger of clinically significant nonadherence.[99] Conversely, using long intervals (i.e., 6–12 months) increases the risk of missing the window of opportunity between the onset of nonadherence and irrevocable treatment failure. Thus, measuring adherence on the order of monthly to quarterly is recommended.

Substance Abuse and ART Adherence

The risk factors in substance abusers are essentially the same as those for non-substance abusers. Barriers to medication adherence emanate from multiple domains. These include personal characteristics, characteristics of the regimen, and cultural and environmental issues. Some, but not all, demographic characteristics are associated with adherence. Older age has been associated with better adherence, perhaps due to a more stable lifestyle with age.[100-102] The association between

gender and adherence may depend on setting and may be confounded by lifestyle. Some studies suggest that HIV-infected women in the developed world have lower rates of adherence than men,[103-105] while in the developing world, the question remains open. Other demographic characteristics, such as race and socioeconomic status, have not been consistently associated with adherence behavior.

Substance abuse itself warrants special attention because it is a strong risk factor for nonadherence.[106-108] These studies focused on active substance use; prior use is not thought to be a risk factor for antiretroviral nonadherence. In contrast, active substance abuse creates a barrier to adherence by impairing judgment, creating a competing priority for money and time to get high rather than pay for and take medications, and, in general, causing a chaotic lifestyle.[109] Also, substance abuse leads to altered sensorium and memory deficits; the issue most commonly cited by patients for nonadherence is forgetting.[110]

The type of substance being abused may influence the degree of risk conferred. Alcohol use has been strongly linked to nonadherence in many different settings, including the developing world.[111-113] Marijuana use has also been associated with nonadherence.[114] Other substances may vary in their impact, depending on the chaos inherent in drug acquisition and subsequent behavior.

Another important barrier to adherence is depression. Substance abusers are at particularly increased risk of depression, since substance abuse may be a form of self-medication for depression and because the social and legal ramifications of substance abuse often result in more difficult life circumstances.[115] Difficult life conditions in susceptible individuals can result in depression. Depressed individuals often have inanition and difficulty coping with activities of daily living, such as medication-taking. Their planning ability (e.g., for obtaining refills) is likewise impaired and may contribute to missed doses.

Health literacy has been found to be associated with nonadherence in the developed world, although the mechanism by which it operates is not clear.[116-117] It may be that people with lower literacy have more trouble negotiating the medical system and thus do not get help when problems accessing medications or coping with side effects arise.[118-120] Or, health literacy may simply be a marker for other social and psychological problems that are the actual barriers to nonadherence.

The relationship between the substance abuser and the health system is typically more complex than for nonabusers.[121-125] Engaging in socially undesirable behaviors often marginalizes substance abusers and is a barrier to access to care. Accordingly, trust in the care provider has been associated with adherence.[126] If the provider is nonjudgmental of substance abuse, the individual may be more likely to acknowledge barriers to adherence, and the provider can help. Further, the nonjudgmental provider may be more willing and more adept at identifying and helping a patient overcome adherence barriers.

Characteristics of the regimen itself can affect adherence. The more times per day a medication is prescribed, the more likely doses will be missed.[127] Most current regimens can be dosed once daily, although not always. Interestingly, while a twice-daily regimen may be associated with a lower proportion of doses taken than a once-daily regimen,[128] the twice-daily regimen may be more forgiving of a missed dose than a once-daily regimen with respect to virological suppression.[129] Adverse drug effects, whether truly caused by the medication or erroneously ascribed to the medication, are often cited by patients as a cause of nonadherence.[130] Gastrointestinal adverse effects (i.e., diarrhea and nausea) and neurological adverse effects (i.e., headache and sleep disturbance) are particularly common with antiretrovirals, and may or may not subside over time. Side effects unique to opiate addicts on methadone maintenance therapy are drug–drug interactions that lower methadone concentrations and precipitate withdrawal symptoms.[131] Therefore, when options exist, patient preference for frequency and number of pills, as well as tolerability, should be accounted for in tailoring a regimen.

Lack of social support is another important risk factor for nonadherence.[132-134] As with substance abuse, HIV infection is stigmatized. Many patients do not disclose their HIV status to anyone other than their medical providers.[135-137] Nondisclosers are therefore isolated with respect to their disease. They lack the encouragement and reminders, as well as the problem-solving help for taking medications that social support would provide. Further, when privacy cannot be assured, hiding medications from others is a barrier to taking them. These patients miss doses at times when taking medications can result in unintended disclosure of HIV status.

In general, adherence in the developing world for those with access to antiretrovirals is higher than in developed-world settings. First, access to antiretrovirals is more limited in developing-world settings, and therefore, those gaining access to medications may have more wherewithal than the population

with easier access in the developed world. Second, the specter of death looms large in the developing world, where in many places life expectancy has dramatically decreased due to AIDS. This makes the benefits of antiretroviral therapy both starker and more proximal to the HIV-infected individual and may help keep antiretroviral adherence a higher priority on the list of competing demands. Yet, certain challenges to adherence are more common in resource-poor settings. These include food insecurity,[138-139] which is a competing demand for time and travel money to access antiretrovirals, even when the medications themselves are free. Pharmacy stockouts140 are a logistical challenge in places where the scale-up of providing antiretroviral therapy has strained infrastructure.

Interventions to Improve Adherence in Drug-Using Populations

Many interventions to improve adherence to antiretrovirals have been tested to date.[141] These include technology-based interventions, behavioral interventions, and combinations of modalities. In general, simpler interventions over shorter periods of time with fewer components have been less successful than more complex and sustained interventions.

The clinical setting is likely an important factor in patient adherence in general, and care sites that provide more services for patients are likely to achieve higher degrees of adherence. Because an understanding of the regimen is certainly necessary for good adherence, an essential starting point for all interventions is the provision of clear information about the expected behavior and the expected effects of the medications, expectations about side effects, and the need for adherence despite difficulties. Provision of memory tools, such as pill organizers, are likely to have modest benefits.[142] Monetary rewards (contingency management) for adherence have some effect, but they are not sustained once payments stop.[143] Simple reminder systems based on cell phone or pager technology have limited to no effect when used alone.[144]

Directly observed therapy (DOT) is one of the best studied modalities. While it may superficially seem to be a simple intervention, DOT consists of a series of components packaged together.[145] These include addressing the logistics of accessing the medications, reminding the patient to take the medications, identifying nonadherence soon after it ensues, and taking action based on the reason for nonadherence (e.g., relapse of substance abuse). A recent meta-analysis concluded that DOT did not have a clinically significant effect in treatment-naïve populations.[146] However, it is possible that higher-risk, drug-abusing populations may benefit from this multifaceted approach.[147] Behavioral approaches such as those based on problem-solving and cognitive behavioral therapy hold promise, but trials are currently ongoing.

Adherence has been referred to as the Achilles' heel of antiretroviral therapy. Although current regimens achieve very high success rates in ideal settings, nonadherence accounts for the major gap between treatment efficacy and effectiveness. Issues that remain to be addressed in substance abusers, in particular, relate to the waxing and waning nature of substance abuse. Forestalling substance abuse relapse is likely to decrease the likelihood of nonadherence. The intermittent nature of the two phenomena (drug craving/seeking behavior and medication nonadherence) call out for real-time monitoring of each to determine whether interventions immediately prior to enactment of the behavior might reduce treatment failure of both problems.

Integration of care for both conditions is also worth exploring. Recently, observational studies on the co-location of HIV and tuberculosis treatment have suggested that outcomes are improved by such logistical arrangements.[148] For example, one can imagine that drug–drug interactions between methadone and antiretroviral drugs would be less common in settings where methadone maintenance and ART services were co-located. Further, the unique issues in substance abusers might be more easily addressed if services were provided together. However, such models have not been formally tested. Other creative technological approaches to treatment monitoring accompanied by real-time behavioral interventions warrant further testing. Although we have a great deal of knowledge regarding the etiology of nonadherence, we lack practical tools to eliminate this ongoing public health problem.

Conclusion

Substance use treatment and prevention remain largely unrecognized as essential components of comprehensive HIV prevention strategies. There has been reluctance to initiate HAART with substance users because of the belief that they would not adhere to HAART, compromising treatment efficacy and promoting HIV drug resistance.[49-50] However, recent evidence demonstrates that these concerns are not warranted, as both substance users and non-substance users have comparable 5-year survival rates on HAART.[54] In addition, concerns regarding the emergence of an epidemic of drug-resistant HIV have not materialized, even in programs that favor aggressive HAART treatment of substance users.[47-48] Comprehensive HAART programs targeting substance users

have been found to be associated with substantial decreases in new HIV infections.[14]

In summary, the available evidence strongly supports the need to rethink the approach to the management of HIV-infected substance users. An aggressive campaign to seek, test, treat, and retain this population will have a significant impact in decreasing substance use and AIDS-related morbidity and mortality, as well as HIV incidence.[149] New policies are urgently needed to support this strategy and overcome individual, provider, and health system barriers to effective integration of substance use prevention and treatment with HIV programs. Ultimately, the HIV/AIDS epidemic cannot be adequately addressed without treating HIV-infected substance users.

Related recommendations made by the breakout groups at the 2010 consultation meeting can be found in Appendix A. They address the following topics: HIV prevention implementation, ART therapy as HIV prevention, human rights, and HIV/AIDS treatment.

References

[1] Fauci, A.S. 25 years of HIV. *Nature* 453, 289–290, 2008.

[2] Carpenter, C.C., Fischl MA, Hammer SM, Hirsch MS, Jacobsen DM, Katzenstein DA, Montaner JS, Richman DD, Sáag MS, Schooley RT, Thompson MA, Vella S, Yeni PG, & Volberding PA. Antiretroviral therapy for HIV infection in 1996: Recommendations of an international panel, International AIDS Society-USA. *JAMA: Journal of the American Medical Association* 276, 146–154, 1996.

[3] British Columbia Centre for Excellence in HIV/AIDS. Antiretroviral Therapy Guidelines. 2009. http://www.cfenet.ubc.ca/our-work/initiatives/therapeutic-guidelines/adult-therapeutic-guidelines.

[4] Hogg, R.S., Heath, K.V., Yip, B., Craib, K.J., O'Shaughnessy, M.V., Schechter, M.T., & Montaner, J. S. Improved survival among HIV-infected individuals following initiation of antiretroviral therapy. *JAMA: Journal of the American Medical Association* 279, 450–454, 1998.

[5] Hogg, R.S., O'Shaughnessy, M.V., Gataric, N., Yip, B., Craib, K., Schechter, M.T., & Montaner, J.S. Decline in deaths from AIDS due to new antiretrovirals. *Lancet* 349, 1294, 1997.

[6] Walensky, R.P., Paltiel, A.D., Losina, E., Mercincavage, L.M., Schackman, B.R., Sax, P.E., Weinstein, M.C., & Freedberg, K.A. The survival benefits of AIDS treatment in the United States. *Journal of Infectious Diseases* 194, 11–19, 2006.

[7] Antiretroviral Therapy Cohort Collaboration. Life expectancy of individuals on combination antiretroviral therapy in high-income countries: A collaborative analysis of 14 cohort studies. *Lancet* 372, 293–299, 2008.

[8] World Health Organization. Towards universal access: Scaling up priority HIV/AIDS interventions in the health sector, Progress Report 2009. 2009. http://www.who.int/hiv/pub/2009progressreport/en/

[9] Braitstein, P., Brinkhof, M.W., Dabis, F., Schechter, M., Boulle, A., Miotti, P., Wood, R., Laurent, C., Sprinz, E., Seyler, C., Bangsberg, D.R., Balestre, E., Sterne, J.A., May, M., Egger, M., the Antiretroviral Therapy in Lower Income Countries (ART-LINC) Collaboration, & the ART Cohort Collaroration (ART_CC). Mortality of HIV-1-infected patients in the first year of antiretroviral therapy: Comparison between low-income and high-income countries. *Lancet* 367, 817–824, 2006.

[10] ART-LINC of leDEA Study Group, Keiser, O., Tweya, H., Boulle, A., Braitstein, P., Schechter, M., Brinkhof, M.W., Dabis, F., Tuboi, S., Sprinz, E., Pujades-Rodriguez, M., Calmy, A., Kumarasamy, N., Nash, D., Jahn, A., MacPhail, P., Luthy, R., Wood, R., & Egger, M. Switching to second-line antiretroviral therapy in resource-limited settings: Comparison of programmes with and without viral load monitoring. *AIDS* 23, 1867–1874, 2009.

[11] Mills, E.J., Nachega, J.B., Buchan, I., Orbinski, J., Attaran, A., Singh, S., Rachlis, B., Wu, P., Cooper, C., Thabane, L., Wilson, K., Guyatt, G.H., & Bangsberg, D.R. Adherence to antiretroviral therapy in sub-Saharan Africa and North America: A meta-analysis. *JAMA: Journal of the American Medical Association* 296, 679–690, 2006.

[12] Centers for Disease Control and Prevention (CDC).Achievements in public health. Reduction in perinatal transmission of HIV infection—United States, 1985–2005. *MMWR Morbidity and Mortality Weekly Repor*t 55, 592–597, 2006.

[13] Attia, S., Egger, M., Muller, M., Zwahlen, M., & Low, N. Sexual transmission of HIV according to viral load and antiretroviral therapy: Systematic review and meta-analysis. *AIDS* 23, 1397–1404, 2009.

[14] Wood, E., Kerr, T., Marshall, B.D., Li, K., Zhang, R., Hogg, R.S., Harrigan, P.R., & Montaner, J.S. Longitudinal community plasma HIV-1 RNA concentrations and incidence of HIV-1 among injecting drug users: Prospective cohort study. *BMJ* 338, b1649, 2009.

[15] Check Hayden, E. "Seek, test and treat" slows HIV. *Nature* 463, 1006, 2010.

[16] Walensky, R.P., Wood, R., Weinstein, M.C., Martinson, N.A., Losina, E., Fofana, M.O., Goldie, S.J., Divi, N., Yazdanpanah, Y., Wang, B., Paltiel, A.D., Freedberg, K.A., & the CEPAC-International Investigators. Scaling up antiretroviral therapy in South Africa: The impact of speed on survival. *Journal of Infectious Diseases* 197, 1324–1332, 2008.

[17] April, M.D., Walensky, R.P., Chang, Y., Pitt, J., Freedberg, K.A., Losina, E., Paltiel, A.D., & Wood, R. HIV testing rates and outcomes in a South African community, 2001–2006: Implications for expanded screening policies. *Journal of Acquired Immune Deficiency Syndromes* 51, 310–316, 2009.

[18] Cohen, M.S., Gay, C., Kashuba, A.D., Blower, S., & Paxton, L. Narrative review: Antiretroviral therapy to prevent the sexual transmission of HIV-1. *Annals of Internal MedicineAnnals of Internal Medicine*146, 591–601, 2007.

[19] Dodd, P.J., Garnett, G.P., & Hallett, T.B. Examining the promise of HIV elimination by 'test and treat' in hyperendemic settings. *AIDS* 24, 729–735, 2010.

[20] Walensky, R.& Kuritzkes, D.R. The impact of the President's Emergency Plan for AIDS Relief (PEPfAR) beyond HIV and why it remains essential. *CID* 50, 272–276, 2009.

[21] Coates, T.J., Richter, L., & Caceres, C. Behavioural strategies to reduce HIV transmission: How to make them work better. *Lancet* 372, 669–684, 2008.

[22] Granich, R., Crowley, S., Vitoria, M., Lo, Y.R., Souteyrand, Y., Dye, C., Gilks, C., Guerma, T., De Cock, K.M., & Williams, B. Highly active antiretroviral treatment for the prevention of HIV transmission. *Journal of the International AIDS Society* 13, 1, 2010.

[23] Gruskin, S. & Tarantola, D. Universal Access to HIV prevention, treatment and care: Assessing the inclusion of human rights in international and national strategic plans. *AIDS* 22 Suppl 2, S123–132, 2008.

[24] Dieffenbach, C.W. & Fauci, A.S. Universal voluntary testing and treatment for prevention of HIV transmission. *JAMA: Journal of the American Medical Association* 301, 2380–2382, 2009.

[25] Wagner, B.G., Kahn, J.S., & Blower, S. Should we try to eliminate HIV epidemics by using a 'Test and Treat' strategy? *AIDS* 24, 775–776, 2010.

[26] Department of Health and Human Services. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. http://www.aidsinfo.nih.gov/guidelines/Default.aspx?MenuItem=Guidelines&Search=On

[27] Hammer, S.M., Eron, J.J. Jr., Reiss, P., Schooley, R.T., Thompson, M.A., Walmsley, S., Cahn, P., Fischl, M.A., Gatell, J.M., Hirsch, M.S., Jacobsen, D.M., Montaner, J.S., Richman, D.D., Yeni, P.G., Volberding, P.A. & the International Aids Society-USA. Antiretroviral treatment of adult HIV infection: 2008 recommendations of the International AIDS Society-USA panel. *JAMA: Journal of the American Medical Association* 300, 555–570, 2008.

[28] Hirsch, M.S. Initiating therapy: When to start, what to use. *Journal of Infectious Diseases* 197 Suppl 3, S252–260, 2008.

[29] D'Agostino, R.B., Sr. The delayed-start study design. *New England Journal of Medicine* 361, 1304–1306, 2009.

[30] Bradford-Hill, A. The environment and disease: Association or Causation? President address at January 14 meeting. *Proceedings of the Royal Society of Medicine* 163, 295–300, 1965.

[31] Blower, S.M., Gershengorn, H.B., & Grant, R.M. A tale of two futures: HIV and antiretroviral therapy in San Francisco. *Science* 287, 650–654, 2000.

[32] Granich, R.M., Gilks, C.F., Dye, C., De Cock, K.M., & Williams, B.G. Universal voluntary HIV testing with immediate antiretroviral therapy as a strategy for elimination of HIV transmission: A mathematical model. *Lancet* 373, 48–57, 2009.

[33] Montaner, J.S., Hogg, R., Wood, E., Kerr, T., Tyndall, M., Levy, A.R., & Harrigan, P.R. The case for expanding access to highly active antiretroviral therapy to curb the growth of the HIV epidemic. *Lancet* 368, 531–536, 2006.

[34] Pao, D., Pillay, D., & Fisher, M. Potential impact of early antiretroviral therapy on transmission. *Current Opinion on HIV and AIDS* 4, 215–221, 2009.

[35] Velasco-Hernandez, J.X., Gershengorn, H.B., & Blower, S.M. Could widespread use of combination antiretroviral therapy eradicate HIV epidemics? *Lancet Infectious Diseases* 2, 487–493, 2002.

[36] Wood, E., Braitstein, P., Montaner, J.S., Schechter, M., Tyndall, M., O'Shaughnessy, M.V., & Hogg, R. Extent to which low-level use of antiretroviral treatment could curb the AIDS epidemic in sub-Saharan Africa. *The Lancet* 355, 2095-2100, 2000.

[37] Cu-Uvin, S., Callendo, A.M., Reinert, S., Chang, A., Juliano-Remollino, C., Flanigan, T.P., Mayer, K.H., & Carpenter, C.C. Effect of highly active antiretroviral therapy on cervicovaginal HIV-1 RNA. *AIDS* 14, 415–421, 2000.

[38] Vernazza, P.L., et al. Effect of antiviral treatment on the shedding of HIV-1 in semen. *AIDS* 11, 1249–1254, 1997.

[39] Lorello, G., la Porte, C., Pilon, R., Zhang, G., Karnauchow, T., & MacPherson, P. Discordance in HIV-1 viral loads and antiretroviral drug concentrations comparing semen and blood plasma. *HIV Medicine* 10, 548–554, 2009.

[40] De Cock, K.M., Fowler, M.G., Mercier, E., de Vincenzi, I., Saba, J., Hoff, E., Alnwick, D.J., Rogers, M., & Shaffer, N. Prevention of mother-to-child HIV transmission in resource-poor countries: Translating research into policy and practice. *JAMA: Journal of the American Medical Association* 283, 1175–1182, 2000.

[41] Piot, P., Bartos, M., Larson, H., Zewdie, D., & Mane, P. Coming to terms with complexity: A call to action for HIV prevention. *Lancet* 372, 845–859, 2008.

[42] HIV Prevention Trials Network.http://www.hptn.org

[43] Fang, C., Hsu, H.M., Twu, S.J., Chen, M.Y., Chang, Y.Y., Hwang, J.S., Wang, J.D., Chuang, C.Y., & the Division of AIDS and STD, Center for Disease Control, Department of Health, Executive Yuan. Decreased HIV transmission after a policy of providing free access to highly active antiretroviral therapy in Taiwan. *Journal of Infectious Diseases* 190, 2004.

[44] Lima, V.D., Johnston, K., Hogg, R.S., Levy, A.R., Harrigan, P.R., Anema, A., & Montaner, J.S.. Expanded access to highly active antiretroviral therapy: A potentially powerful strategy to curb the growth of the HIV epidemic. *Journal of Infectious Diseases* 198, 59–67, 2008.

[45] Tam, L.W., Chui, C.K., Brumme, C.J., Bangsberg, D.R., Montaner, J.S., Hogg, R.S., & Harrigan, P.R. The relationship between resistance and adherence in drug-naive individuals initiating HAART is specific to individual drug classes. *Journal of Acquired Immune Deficiency Syndromes* 49, 266–271, 2008.

[46] Buckheit, R.W., Jr. Understanding HIV resistance, fitness, replication capacity and compensation: Targeting viral fitness as a therapeutic strategy. *Expert Opin Investig Drugs* 13, 933–958, 2004.

[47] Wood, E., Hogg, R.S., Yip, B., Dong, W.W., Wynhoven, B., Mo, T., Brumme, C.J., Montaner, J.S., & Harrigan, P. R. Rates of antiretroviral resistance among HIV-infected patients with and without a history of injection drug use. *AIDS* 19, 1189–1195, 2005.

[48] Gill, V.S., Lima, V.D., Zhang, W., Wynhoven, B., Yip, B., Hogg, R.S., Montaner, J.S., Harrigan, P. R. Improved virological outcomes in British Columbia concomitant with decreasing incidence of HIV type 1 drug resistance detection. *Clinical Infectious Diseases* 50, 98–105, 2010.

[49] Chander, G., Himelhoch, S., & Moore, R.D. Substance abuse and psychiatric disorders in HIV-positive patients: Epidemiology and impact on antiretroviral therapy. *Drugs* 66, 769–789, 2006.

[50] Lert, F. & Kazatchkine, M.D. Antiretroviral HIV treatment and care for injecting drug users: An evidence-based overview. *International Journal of Drug Policy* 18, 255–261, 2007.

[51] Wood, E., Kerr, T. & Montaner, J.S. HIV treatment, injection drug use, and illicit drug policies. *Lancet* 370, 8–10, 2007.

[52] Bruce, R.D. & Altice, F.L. Clinical care of the HIV-infected drug user. *Infectious Disease Clinics of North America* 21, 149–179, ix, 2007.

[53] Wood, E., Montaner, J.S., Tyndall, M.W., Schechter, M.T., O'Shaughnessy, M.V., & Hogg, R.S.. Prevalence and correlates of untreated human immunodeficiency virus type 1 infection among persons who have died in the era of modern antiretroviral therapy. *Journal of Infectious Diseases* 188, 1164–1170, 2003.

[54] Wood, E., Hogg, R.S., Lima, V.D., Kerr, T., Yip, B., Marshall, B.D., & Montaner, J.S. Highly active antiretroviral therapy and survival in HIV-infected injection drug users. *JAMA: Journal of the American Medical Association* 300, 550–554, 2008.

[55] Substance Abuse and Mental Health Services Administration. Office of Applied Studies. National Survey of Substance Abuse Treatment Services (N-SSATS):2007. Data on Substance Abuse Treatment Facilities. (ed. Services, D.o.H.a.H.) (Rockville, MD, 2007). http://oas.samhsa.gov/dasis.htm#nssats3

[56] Brown, L.S., Jr., Kritz S., Chu M., & Madray C. Characteristics of substance abuse treatment programs providing services for HIV/AIDS, hepatitis C virus infection, and sexually transmitted infections: The National Drug Abuse Treatment Clinical Trials Network. *Journal of Substance Abuse Treatment* 30, 315–321, 2006.

[57] Centers for Disease Control and Prevention (CDC). Persons tested for HIV—United States, 2006. *MMWR Morbidity and Mortality Weekly Report* 57, 845–849, 2008.

[58] Bhaskaran, K., Hamouda, O., Sannes, M., Boufassa, F., Johnson, A.M., Lambert, P.C., Porter, K., & the CASCADE Collaboration. Changes in the risk of death after HIV seroconversion compared with mortality in the general population. *JAMA: Journal of the American Medical Association* 300, 51–59, 2008.

[59] Harrison, K.M., Song, R., & Zhang, X. Life expectancy after HIV diagnosis based on national HIV surveillance data from 25 states, United States. *Journal of Acquired Immune Deficiency Syndromes* 53, 124–130, 2010.

[60] Gazzard, B.G., Anderson, J., Babiker, A., Boffito, M., Brook, G., Brough, G., Churchill, D., Cromarty, B., Das, S., Fisher, M., Freedman, A., Geretti, A.M., Johnson, M., Khoo, S., Leen, C., Nair, D., Peters, B., Phillips, A., Pillay, D., Pozniak, A., Walsh, J., Wilkins, E., Williams, I., Williams, M. Youle, M., & the BHIVA Treatment Guidelines Wrigint Group. British HIV Association Guidelines for the treatment of HIV-1-infected adults with antiretroviral therapy 2008. *HIV Medicine* 9, 563–608, 2008.

[61] European AIDS Clinical Society Guidelines: Clinical management and Treatment of HIV infected Adults in Europe http://www.europeanaidsclinicalsociety.org/guidelines.asp

[62] Panel on Clinical Practices for the Treatment of HIV Infection. Guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents. 2009.

[63] World Health Organization. WHO Revisions to WHO guidelines for antiretroviral treatment of adults and adolescents. 2009. http://www.who.int/hiv/pub/arv/advice/en/index.html

[64] Fischl, M.A., Richman, D.D., Grieco, M.H., Gottlieb, M.S., Volberding, P.A., Laskin, O.L., Leedom, J.M., Groopman, J.E., Mildvan, & D., Schooley, R.T. The efficacy of azidothymidine (AZT) in the treatment of patients with AIDS and AIDS-related complex. A double-blind, placebo-controlled trial. *New England Journal of Medicine* 317, 185–191, 1987.

[65] Montaner, J.S., Reiss, P., Cooper, D., Vella, S., Harris, M., Conway, B., Wainberg, M.A., Smith, D., Robinson, P., Hall, D., Myers, M. & Lange, J. M. A randomized, double-blind trial comparing combinations of nevirapine, didanosine, and zidovudine for HIV-infected patients: The INCAS Trial. Italy, The Netherlands, Canada and Australia Study. *JAMA: Journal of the American Medical Association* 279, 930–937, 1998.

[66] Staszewski, S., Morales-Ramirez, J., Tashima, K.T., Rachlis, A., Skiest, D., Stanford, J., Stryker, R., Johnson, P., Labriola, D.F., Farina, D., Manion, D.J., & Ruiz, N.M. Efavirenz plus zidovudine and lamivudine, efavirenz plus indinavir, and indinavir plus zidovudine and lamivudine in the treatment of HIV-1 infection in adults. Study 006 Team. *New England Journal of Medicine* 341, 1865–1873, 1999.

[67] Cameron, D.W., Heath-Chiozzi, M., Danner, S., Cohen, C., Kravcik, S., Maurath, C., Sun, E., Henry, D., Rode, R., Potthoff, A., & Leonard, J. Randomised placebo-controlled trial of ritonavir in advanced HIV-1 disease. The Advanced HIV Disease Ritonavir Study Group. *Lancet* 351, 543–549, 1998.

[68] Gulick, R.M., Mellors, J.W., Havlir,D., Eron, J.J., Gonzalez, C., McMahon, D., Richman, D.D., Valentine, F.T., Jonas, L., Meibohm, A., Emini, E.A., & Chodakewitz, J.A. Treatment with indinavir, zidovudine, and lamivudine in adults with human immunodeficiency virus infection and prior antiretroviral therapy. *New England Journal of Medicine* 337, 734–739, 1997.

[69] Hammer, S.M., Squires, K.E., Hughes, M.D., Grimes, J.M., Demeter, L.M., Currier, J.S., Eron, J.J. Jr., Feinberg, J.E., Balfour, H.H. Jr., Deyton, L.R., Chodakewitz, J.A., & Fischl, M. A. A controlled trial of two nucleoside analogues plus indinavir in persons with human immunodeficiency virus infection and CD4 cell counts of 200 per cubic millimeter or less. AIDS Clinical Trials Group 320 Study Team. *New England Journal of Medicine* 337, 725–733, 1997.

[70] Lalezari, J.P., Henry, K., O'Hearn, M., Montaner, J.S., Piliero, P.J. Trottier, B., Walmsley, S., Cohen, C., Kuritzkes, D.R., Eron, J.J. Jr., Chung, J., DeMasi, R., Donatacci, L., Drobnes, C., Delehanty, J., Salgo, M. & the TORO 1 Study Group. Enfuvirtide, an HIV-1 fusion inhibitor, for drug-resistant HIV infection in North and South America. *New England Journal of Medicine* 348, 2175–2185, 2003.

[71] Lazzarin, A., Clotet, B., Cooper, D., Reynes, J., Arasten, K., Nelson, M., Katlama, C., Stellbrink, H.J., Delfraissy, J.F., Lange, J., Huson, L., DeMasi, R., Wat, C., Delehanty, J., Drobnes, C., Salgo, M., & the TORO 2 Study Group. Efficacy of enfuvirtide in patients infected with drug-resistant HIV-1 in Europe and Australia. *New England Journal of Medicine* 348, 2186–2195, 2003.

[72] Fatkenheuer, G., Nelson, M., Lazzarin, A., Konourina, I., Hoepelman, A.I., Lampiris, H., Hirschel, B., Tebas, P., Raffi, F., Trottier, B., Bellos, N., Saag, M., Cooper, D.A., Westby, M., Tawadrous, M., Sullivan, J.F., Ridgway, C., Dunne, M.W., Felstead, S., Mayer, H., van der Ryst, E. & the MOTIVATE 1 and MOTIVATE 2 Study Teams. Subgroup analyses of maraviroc in previously treated R5 HIV-1 infection. *New England Journal of Medicine* 359, 1442–1455, 2008.

[73] Gulick, R.M., Lalezari, J., Goodrich, J., Clumeck, N., DeJesus, E., Horban, A., Nadler, J., Clotet, B., Karlsson, A., Wohlfeiler, M., Montana, J.B., McHale, M., Sullivan, J., Ridgway, C., Felstead, S., Dunne, M.W., van der Ryst E., Mayer, H. & the MOTIVATE Study Teams. Maraviroc for previously treated patients with R5 HIV-1 infection. *New England Journal of Medicine* 359, 1429–1441, 2008.

[74] Cooper, D.A., Steigbigel, R.T., Gattell, J.M., Rockstroh, J.K., Katlama, C., Yeni, P., Lazzarin, A., Clotet, B., Kumar, P.N., Eron, J.E., Schechter, M., Markowitz, M., Loulfy, M.R., Lennox, J.L., Zhao, J., Chen, J., Ryan, D.M., Rhodes, R.R., Kilar, J.A., Gilde, L.R., Strohmaier, K.M., Meibohm, A.R., Miller, M.D., Hazuda, D.J., Nessly, M.L., DiNubile, M.J., Isaacs, R.D., Teppler, H., Nguyen, B.Y., & the BENCHMRK Study Teams. Subgroup and resistance analyses of raltegravir for resistant HIV-1 infection. *New England Journal of Medicine* 359, 355–365, 2008.

[75] Steigbigel, R.T., Cooper, D.A., Kumar, P.N., Eron, J.E., Schechter, M., Markowitz, M., Loulfy, M.R., Lennox, J.L., Rockstroh, J.K., Katlama, C., Yeni, P., Lazzarin, A., Clotet, B., Zhao, J., Chen, J., Ryan, D.M., Rhodes, R.R., Killar, J.A., Glide, L.R., Strohmaier, K.M., Meibohm, A.R., Miller, M.D., Nessly, M.L., DiNubile, M.J., Isaacs, R.D., Nguyen, B.Y., Teppler, H., & the BENCHMRK Study Teams. Raltegravir with optimized background therapy for resistant HIV-1 infection. *New England Journal of Medicine* 359, 339–354, 2008.

[76] Marais, S., Wilkinson, R.J., Pepper, D.J., & Meintjes, G. Management of patients with the immune reconstitution inflammatory syndrome. *Current HIV/AIDS Reports* 6, 162–171, 2009.

[77] DART Trial Team, Mugyenyi, P., Walker, A.S., Hakim, J., et al. Routine versus clinically driven laboratory monitoring of HIV antiretroviral therapy in Africa (DART): A randomised non-inferiority trial. *Lancet* 375, 123–131, 2010.

[78] Coutinho, A., Mermin, J., Ekwaru, J., Were, W., Bunnell, R., Kaharuza, F., Alexander, L., Solberg, P., Tappero, J., & Moore, D. Utility of Routine Viral Load, CD4 Cell Count, and Clinical Monitoring Among HIV-Infected Adults in Uganda: A Randomized Trial[125]. In *15th Conference on Retroviruses and Opportunistic Infections*. Boston, 2008.

[79] Bangsberg, D.R., Hecht, F.M., Charlebois, E.D., Zolopa, A.R., Holodniy, M., Sheiner, L., Bamberger, J.D., Chesney, M.A., & Moss, A. Adherence to protease inhibitors, HIV-1 viral load, and development of drug resistance in an indigent population. *AIDS* 14, 357–366, 2000.

[80] Bangsberg, D.R., Perry, S., Charlebois, E.D., Clark, R.A., Robertson, M., Zolopa, A.R., & Moss, A. Non-adherence to highly active antiretroviral therapy predicts progression to AIDS. *AIDS* 15, 1181–1183, 2001.

[81] Nachega, J.B., Hislop, M., Dowdy, D.W., Lo, M., Omer, S.B., Regensberg, L., Chaisson, R.E., & Maartens, G. Adherence to highly active antiretroviral therapy assessed by pharmacy claims predicts survival in HIV-infected South African adults. *Journal of Acquired Immune Deficiency Syndromes* 43, 78–84, 2006.

[82] Paterson, D.L., Swindells, S., Mohr, J., Brester, M., Vergis, E.N., Squier, C., Wagener, M.M., & Singh, N. Adherence to protease inhibitor therapy and outcomes in patients with HIV infection. *Annals of Internal Medicine* 133, 21–30, 2000.

[83] Wood, E., Hogg, R.S., Yip, B., Harrigan, P.R., O'Shaughnessy, M.V., & Montaner, J.S. The impact of adherence on CD4 cell count responses among HIV-infected patients. *Journal of Acquired Immune Deficiency Syndromes* 35, 261–268, 2004.

[84] Lima, V.D., Harrigan, R., Bangsberg, D.R., Hogg, R.S., Gross, R., Yip, B., & Montaner, J. S. The combined effect of modern highly active antiretroviral therapy regimens and adherence on mortality over time. *Journal of Acquired Immune Deficiency Syndromes* 50, 529–536, 2009.

[85] Wood, E., Hogg, R.S., Yip, B., Harrigan, P.R., O'Shaughnessy, M.V., & Montaner, J. S. Effect of medication adherence on survival of HIV-infected adults who start highly active antiretroviral therapy when the CD4+ cell count is 0.200 to 0.350 x 10(9) cells/L. *Annals of Internal Medicine* 139, 810–816, 2003.

[86] Alexander, C.S., Asselin J.J., Ting, L.S., Montaner, J.S., Hogg, R.S., Yip, B., O'Shaughnessy, M.V., & Harrigan, P.R. Antiretroviral concentrations in untimed plasma samples predict therapy outcome in a population with advanced disease. *Journal of Infectious Diseases* 188, 541–548, 2003.

[87] Bangsberg, D.R., Acosta, E.P., Gupta, R., Guzman, D., Riley, E.D., Harrigan, P.R., Parkin, N., & Deeks, S.G. Adherence-resistance relationships for protease and non-nucleoside reverse transcriptase inhibitors explained by virological fitness. *AIDS* 20, 223–231, 2006.

[88] Gardner, E.M., Burman, W.J., Steiner, J.F., Anderson, P.L., & Bangsberg, D.R. Antiretroviral medication adherence and the development of class-specific antiretroviral resistance. *AIDS* 23, 1035–1046, 2009.

[89] Lockman, S., Shapiro, R.L., Smeaton, L.M., Wester, C., Thior, I., Stevens, L., Chand, F., Makhema, J., Moffat, C., Asmelash, A., Ndase, P., Arimi, P., van Widenfelt, E., Mazhani, L. Novitsky, V., Lagakos, S. & Essex, M. Response to antiretroviral therapy after a single, peripartum dose of nevirapine. *New England Journal of Medicine* 356, 135–147, 2007.

[90] Simoni, J.M., Kurth, A.E., Pearson, C.R., Pantalone, D.W., Merrill, J.O., & Frick, P.A. Self-report measures of antiretroviral therapy adherence: A review with recommendations for HIV research and clinical management. *AIDS Behav* 10, 227–245, 2006.

[91] Grossberg, R., Zhang, Y., & Gross, R. A time-to-prescription-refill measure of antiretroviral adherence predicted changes in viral load in HIV. *Journal of Clinical Epidemiology* 57, 1107–1110, 2004.

[92] Low-Beer, S., Yip, B., O'Shaughnessy, M.V., Hogg, R.S., & Montaner, J.S. Adherence to triple therapy and viral load response. *Journal of Acquired Immune Deficiency Syndromes* 23, 360–361, 2000.

[93] Nachega, J.B., Hislop, M., Dowdy, D.W., Gallant, J.E., Chaisson, R.E., Regensberg, L., & Maartens, G. Efavirenz versus nevirapine-based initial treatment of HIV infection: Clinical and virological outcomes in Southern African adults. *AIDS* 22, 2117–2125, 2008.

[94] Berg, K.M. & Arnsten, J.H. Practical and conceptual challenges in measuring antiretroviral adherence. *Journal of Acquired Immune Deficiency Syndromes* 43 Suppl 1, S79–87, 2006.

[95] Gandhi, M., Ameli, N., Bacchetti, P., Gange, S.J., Anastos, K., Levine, A., Hyman, C.L., Cohen, M., Young, M., Huang, Y., Greenblatt, R.M. & the Women's Interagency HIV Study (WIHS). Protease inhibitor levels in hair strongly predict virologic response to treatment. *AIDS* 23, 471–478, 2009.

[96] Yasuda, J.M., Miller, C., Currier, J.S., Forthal, D.N., Kemper, C.A., Beall, G.N., Tilles, J.G., Capparelli, E.V., McCutchan, J.A., Haubrich, R.H. & the California Collaborative Treatment Grouup. The correlation between plasma concentrations of protease inhibitors, medication adherence and virological outcome in HIV-infected patients. *Antiviral Therapy* 9, 753–761, 2004.

[97] Gross, R., Yip, B., Lo Re, V. 3rd, Wood, E., Alexander, C.S., Harrigan, P.R., Bangsberg, D.R., Montaner, J.S., & Hogg, R.S. A simple, dynamic measure of antiretroviral therapy adherence predicts failure to maintain HIV-1 suppression. *Journal of Infectious Diseases* 194, 1108–1114, 2006.

[98] Gross, R., Bilker, W.B., Wang, H., & Chapman, J. How long is the window of opportunity between adherence failure and virologic failure on efavirenz-based HAART? *HIV Clinical Trials* 9, 202–206, 2008.

[99] Parienti, J.J., Das-Douglas, M., Masari, V., Guzman, D., Deeks, S.G., Verdon, R., & Bangsberg, D.R. Not all missed doses are the same: Sustained NNRTI treatment interruptions predict HIV rebound at low-to-moderate adherence levels. *PLoS One* 3, e2783, 2008.

[100] Barclay, T.R., Hinkin, C.H., Castellon, S.A., Mason, K.I., Reinhard, M.J., Marion, S.D., Levine, A.J., & Durvasula, R.S. Age-associated predictors of medication adherence in HIV-positive adults: Health beliefs, self-efficacy, and neurocognitive status. *Health Psychol* 26, 40–49, 2007.

[101] Hinkin, C.H., Hardy, D.J., Mason, K.I., Castellon, S.A., Durvasula, R.S., Lam, M.N., & Stefaniak, M. Medication adherence in HIV-infected adults: Effect of patient age, cognitive status, and substance abuse. *AIDS* 18 Suppl 1, S19–25, 2004.

[102] Silverberg, M.J., Leyden, W., Horberg, M.A., DeLorenze, G.N., Klein, D., & Quesenberry, C.P. Jr. Older age and the response to and tolerability of antiretroviral therapy. *Archives of Internal Medicine* 167, 684–691, 2007.

[103] Berg, K.M., Demas, P.A., Howard, A.A., Schoenbaum, E.E., Gourevitch, M.N., & Arnsten, J.H. Gender differences in factors associated with adherence to antiretroviral therapy. *Journal of General Internal Medicine* 19, 1111–1117, 2004.

[104] Kuyper, L.M., Wood, E., Montaner, J.S., Yip, B., O'Connell, J.M., & Hogg, R.S. Gender differences in HIV-1 RNA rebound attributed to incomplete antiretroviral adherence among HIV-Infected patients in a population-based cohort. *Journal of Acquired Immune Deficiency Syndromes* 37, 1470–1476, 2004.

[105] Nicastri, E., Leone, S., Angeletti, C., Palmisano, L., Sarmati, L., Chiesi, A., Geraci, A., Vella, S., Narciso, P., Corpolongo, A. & Andreoni, M. Sex issues in HIV-1-infected persons during highly active antiretroviral therapy: A systematic review. *Journal of Antimicrobial Chemotherapy* 60, 724–732, 2007.

[106] Bouhnik, A.D., Chesney, M., Carrieri, P., Gallais, H., Moreau, J., Moatti, J.P., Obadia, Y., Spire, B., & the MANIF 2000 Study Group. Nonadherence among HIV-infected injecting drug users: The impact of social instability. *Journal of Acquired Immune Deficiency Syndromes* 31 Suppl 3, S149–153, 2002.

[107] Golin, C.E., Liu, H., Hays, R.D., Miller, L.G., Beck, C.K., Ickovisc, J., Kapan, A.H., & Wenger, N.S. A prospective study of predictors of adherence to combination antiretroviral medication. *Journal of General Internal Medicine* 17, 756–765, 2002.

[108] Lucas, G.M., Cheever, L.W., Chaisson, R.E., & Moore, R.D. Detrimental effects of continued illicit drug use on the treatment of HIV-1 infection. *Journal of Acquired Immune Deficiency Syndromes* 27, 251–259, 2001.

[109] Rosen, M.I., Rigsby, M.O., Dieckhaus, K.D., & Cramer, J.A. Effects of illicit drug use on adherence to prescribed antiretroviral medication. *American Journal of Addiction* 12, 455–458, 2003.

[110] Reynolds, N.R., Testa, M.A., Marc, L.G., Chesney, M.A., Neidig, J.L., Smith, S.R., Vella, S., Robbins, G.K., and the Protocol Teams of ACTG 384, ACTG 731 and A5031s. Factors influencing medication adherence beliefs and self-efficacy in persons naive to antiretroviral therapy: A multicenter, cross-sectional study. *AIDS and Behavior* 8, 141–150, 2004.

[111] Braithwaite, R.S., McGinnis, K.A., Conigliaro, J., Maisto, S.A., Crystal, S., Day, N., Cook, R.L., Gordon, A., Bridges, M.W., Seller, J.F. & Justice A.C. A temporal and dose-response association between alcohol consumption and medication adherence among veterans in care. *Alcoholism: Clinical Experimental Research* 29, 1190–1197, 2005.

[112] Chander, G., Lau, B., & Moore, R.D. Hazardous alcohol use: A risk factor for non-adherence and lack of suppression in HIV infection. *Journal of Acquired Immune Deficiency Syndromes* 43, 411–417, 2006.

[113] Dahab, M., Charalambous, S., Hamilton, R., Fielding, K., Kielmann, K., Churchyard, G.J., & Grant, A.D. "That is why I stopped the ART": Patients' & providers' perspectives on barriers to and enablers of HIV treatment adherence in a South African workplace programme. *BMC Public Health* 8, 63, 2008.

[114] Holmes, W.C., Bilker, W.B., Wang, H., Chapman, J., & Gross, R. HIV/AIDS-specific quality of life and adherence to antiretroviral therapy over time. *Journal of Acquired Immune Deficiency Syndromes* 46, 323–327, 2007.

[115] Lima, V.D., Geller, J., Bangsberg, D.R., Patterson, T.L., Daniel, M., Kerr, T., Montaner, J.S., & Hogg, R.S. The effect of adherence on the association between depressive symptoms and mortality among HIV-infected individuals first initiating HAART. *AIDS* 21, 1175–1183, 2007.

[116] Graham, J., Bennett, I.M., Holmes, W.C., & Gross, R. Medication beliefs as mediators of the health literacy-antiretroviral adherence relationship in HIV-infected individuals. *AIDS and Behavior* 11, 385–392, 2007.

[117] Kalichman, S.C., Ramachandran, B., & Catz, S. Adherence to combination antiretroviral therapies in HIV patients of low health literacy. *Journal of General Internal Medicine* 14, 267–273, 1999.

[118] Kalichman, S.C., Benotsch, E., Suarez, T., Catz, S., Miller, J., & Rompa, D. Health literacy and health-related knowledge among persons living with HIV/AIDS. *American Journal of Preventive Medicine* 18, 325–331, 2000.

[119] Kalichman, S.C. & Rompa, D. Functional health literacy is associated with health status and health-related knowledge in people living with HIV-AIDS. *Journal of Acquired Immune Deficiency Syndromes* 25, 337–344, 2000.

[120] Wolf, M.S., Davis, T.C., Arozullah, A., Penn, R., Arnold, C., Sugar, M., & Bennett, C.L. Relation between literacy and HIV treatment knowledge among patients on HAART regimens. *AIDS Care* 17, 863–873, 2005.

[121] Carrieri, M.P., Moatti, J.P., Vlahov, D., Obadia, Y., Reynaud-Maurupt, C., & Chesney, M. Access to antiretroviral treatment among French HIV infected injection drug users: The influence of continued drug use. MANIF 2000 Study Group. *Journal of Epidemiological Community Health* 53, 4–8, 1999.

[122] Grigoryan, A., Hall, H.I., Durant, T., & Wei, X. Late HIV diagnosis and determinants of progression to AIDS or death after HIV diagnosis among injection drug users, 33 US States, 1996–2004. *PLoS One* 4, e4445, 2009.

[123] Murri, R., Fantoni, M., Del Borgo, C., Izzi, I., Visona, R., Suter, F., Banfi, M.C., Barchi, E., Orchi, N., Bosco, O., & Wu, A.W.. Intravenous drug use, relationship with providers, and stage of HIV disease influence the prescription rates of protease inhibitors. *Journal of Acquired Immune Deficiency Syndromes* 22, 461–466, 1999.

[124] Wood, E., Kerr, T., Palepu, A., Zhang, R., Strathdee, S.A., Tyndall, M.W., Montaner, J.S., & Hogg, R.S. Slower uptake of HIV antiretroviral therapy among Aboriginal injection drug users. *Journal of Infection* 52, 233–236, 2006.

[125] Wood, E., Kerr, T., Zhang, R., Guillemi, S., Palepu, A., Hogg, R.S., & Montaner, J.S. Poor adherence to HIV monitoring and treatment guidelines for HIV-infected injection drug users. *HIV Medicine* 9, 503–507, 2008.

[126] Mostashari, F., Riley, E., Selwyn, P.A., & Altice, F.L. Acceptance and adherence with antiretroviral therapy among HIV-infected women in a correctional facility. *Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology* 18, 341–348, 1998.

[127] Ingersoll, K.S. & Cohen, J. The impact of medication regimen factors on adherence to chronic treatment: A review of literature. *Journal of Behavioral Medicine* 31, 213–224, 2008.

[128] Parienti, J.J., Bangsberg, D.R., Verdon, R., & Gardner, E.M. Better adherence with once-daily antiretroviral regimens: A meta-analysis. *Clinical Infectious Diseases* 48, 484–488, 2009.

[129] Flexner, C., Tierney, C., Gross, R., Andrade, A., Lalama, C., Eshleman, S.H., Aberg, J., Sanne, I., Parsons, T. Kashuba, A., Rosenkranz, S.L., Kmack, A., Ferguson, E., Dehlinger, M., Mildvan, D. & the ACTG A5073 Study Team. Comparison of once-daily versus twice-daily combination antiretroviral therapy in treatment-naive patients: Results of AIDS clinical trials group (ACTG) A5073, a 48-week randomized controlled trial. *Clinical Infectious Diseases* 50, 1041–1052, 2010.

[130] Sullivan, P.S., Campsmith, M.L., Nakamura, G.V., Begley, E.B., Schulden, J., & Nakashima, A.K. Patient and regimen characteristics associated with self-reported nonadherence to antiretroviral therapy. *PLoS One* 2, e552, 2007.

[131] Altice, F.L., Friedland, G.H., & Cooney, E.L. Nevirapine induced opiate withdrawal among injection drug users with HIV infection receiving methadone. *AIDS* 13, 957–962, 1999.

[132] Carrieri, M.P., Leport, C., Protopopescu, C., Cassuto, J.P., Bouvet, E., Peyarmond, D., Raffi, F., Moatti, J.P., Chene G., & Spire, B. Factors associated with nonadherence to highly active antiretroviral therapy: A 5-year follow-up analysis with correction for the bias induced by missing data in the treatment maintenance phase. *Journal of Acquired Immune Deficiency Syndromes* 41, 477–485, 2006.

[133] Catz, S.L., Kelly, J.A., Bogart, L.M., Benotsch, E.G., & McAuliffe, T.L. Patterns, correlates, and barriers to medication adherence among persons prescribed new treatments for HIV disease. *Health Psychology* 19, 124–133, 2000.

[134] Gordillo, V., del Amo, J., Soriano, V., & Gonzalez-Lahoz, J. Sociodemographic and psychological variables influencing adherence to antiretroviral therapy. *AIDS* 13, 1763–1769, 1999.

[135] Bajunirwe, F., Arts, E.J., Tisch, D.J., King, C.H., Debanne, S.M., & Sethi, A.K. Adherence and treatment response among HIV-1-infected adults receiving antiretroviral therapy in a rural government hospital in Southwestern Uganda. *Journal of International Association of Physicians in AIDS Care* (Chic Ill) 8, 139–147, 2009.

[136] Ramadhani, H.O., Thielman, N.M., Landman, K.Z., Ndosi, E.M., Gao, F., Kirchherr, J.L., Shah, R., Shao, H.J., Morpeth, S.C., McNeill, J.D., Shao, J.F., Bartlett, J.A., & Crump, J.A. Predictors of incomplete adherence, virologic failure, and antiviral drug resistance among HIV-infected adults receiving antiretroviral therapy in Tanzania. *Clinical Infectious Diseases* 45, 1492–1498, 2007.

[137] Wouters, E., van Loon, F., van Rensburg, D., & Meulemans, H. Community support and disclosure of HIV serostatus to family members by public-sector antiretroviral treatment patients in the Free State Province of South Africa. *AIDS Patient Care STDS* 23, 357–364, 2009.

[138] Weiser, S.D., Fernandes, K.A., Brandson, E.K., Lima, V.D., Anema, A., Bangsberg, D.R., Montaner, J.S., & Hogg, R.S.. The association between food insecurity and mortality among HIV-infected individuals on HAART. *Journal of Acquired Immune Deficiency Syndromes* 52, 342–349, 2009.

[139] Weiser, S.D., Frongillo, E.A., Ragland, K., Hogg, R.S., Riley, E.D., & Bangsberg, D.R.. Food insecurity is associated with incomplete HIV RNA suppression among homeless and marginally housed HIV-infected individuals in San Francisco. *Journal of General Internal Medicine* 24, 14–20, 2009.

[140] Byakika-Tusiime, J., Oyugi, J.H., Tumwikirize, W.A., Katabira, E.T., Mugyenyi, P.N., & Bangsberg, D.R. Adherence to HIV antiretroviral therapy in HIV+ Ugandan patients purchasing therapy. *International Journal of STD & AIDS* 16, 38–41, 2005.

[141] Simoni, J.M., Amico, K.R., Pearson, C.R., & Malow, R. Strategies for promoting adherence to antiretroviral therapy: A review of the literature. *Current Infectious Disease Reports* 10, 515–521, 2008.

[142] Petersen, M.L., Wang, Y., van der Laan, M.J., Guzman, D., Riley, E., & Bangsberg, D.R. Pillbox organizers are associated with improved adherence to HIV antiretroviral therapy and viral suppression: A marginal structural model analysis. *Clinical Infectious Diseases* 45, 908–915, 2007.

[143] Rigsby, M.O., Rosen, M.I., Beauvais, J.E., Cramer, J.A., Rainey, P.M., O'Malley, S.S., Dieckhaus, K.D., & Rounsaville, B.J. Cue-dose training with monetary reinforcement: Pilot study of an antiretroviral adherence intervention. *Journal of General Internal Medicine* 15, 841–847, 2000.

[144] Simoni, J.M., Huh, D., Frick, P.A., Pearson, C.R., Andrasik, M.P., Dunbar, P.J., & Hooton, T.M. Peer support and pager messaging to promote antiretroviral modifying therapy in Seattle: A randomized controlled trial. *Journal of Acquired Immune Deficiency Syndromes* 52, 465–473, 2009.

[145] Volmink, J., Matchaba, P., & Garner, P. Directly observed therapy and treatment adherence. *Lancet* 355, 1345–1350, 2000.

[146] Ford, N., Nachega, J.B., Engel, M.E., & Mills, E.J. Directly observed antiretroviral therapy: A systematic review and meta-analysis of randomised clinical trials. *Lancet* 374, 2064–2071, 2009.

[147] Altice, F.L., Maru, D.S., Bruce, R.D., Springer, S.A., & Friedland, G.H. Superiority of directly administered antiretroviral therapy over self-administered therapy among HIV-infected drug users: A prospective, randomized, controlled trial. *Clinical Infectious Diseases* 45, 770–778, 2007.

[148] Gandhi, N.R., Moll, A.P., Lalloo, U., Pawnski, R., Zeller, K., Moodley, P., Meyer, E., Friedland, G., & the Tugela Ferry Care and Research (TFCaRes) Collaboration. Successful integration of tuberculosis and HIV treatment in rural South Africa: The Sizonq'oba study. *Journal of Acquired Immune Deficiency Syndromes* 50, 37–43, 2009.

[149] Volkow, N.D., & Montaner, J. Enhanced HIV testing, treatment, and support for HIV-infected substance users. *JAMA: Journal of the American Medical Association* 303, 1423-1424, 2010.

Chapter 5. Drug Abuse, HIV/AIDS, and the Criminal Justice System: Challenges and Opportunities

There is frequently a dichotomy in how drug abuse and addiction are viewed by those with a public health background versus those in the field of criminal justice. Those with a public health orientation view drug abuse and addiction as a chronic, relapsing brain disease.[1] The law enforcement/criminal justice perspective, on the other hand, tends to view drug abusers as individuals who should be isolated, controlled, and contained because of their involvement in illegal activities, even though they frequently are incarcerated for nonviolent drug crimes.[2-3] As a result of the predominance of the law enforcement perspective, drug abusers, including injection drug users (IDUs), are overrepresented in criminal justice populations in the U.S. and internationally[4-7] Rates of HIV infection in prisons also are elevated relative to the general population in much of the world. In many regions of the world, this disparity reflects high rates of incarceration of IDUs and high prevalence of HIV among IDUs.[4,6] It has been argued that, particularly among sex workers and IDUs, incarceration itself is a driver of the global HIV epidemic.[8]

The high numbers of drug users involved in criminal justice systems presents both challenges and opportunities. The challenges are reflected in policies that prevent implementation of appropriate drug abuse treatment and HIV/AIDS services for prisoners that would improve their health and safeguard the health of their communities upon their release. The missed opportunities are for effective diagnosis, treatment, linkage to care, and prevention within the criminal justice system, and discharge planning and linkage to care in the community. This section will explore the high rates of incarceration among drug abusers and how this has led to unintended adverse consequences for their health and the health of their communities. It will then describe promising approaches for utilizing the criminal justice system as a means of delivering public health interventions.

The "War on Drugs" and Increased Incarceration of Drug Abusers

The U.S. "War on Drugs," a set of laws and policies intended to discourage the production, distribution, and consumption of illicit drugs that was first promulgated by President Richard Nixon,[9] has led to the U.S. having the highest incarceration rate in the world, with over 2.3 million people in prisons and jails, or approximately 750 inmates per 100,000 residents.[10-11] In 2008, more than 7.3 million people were involved with the criminal justice system, representing 3.2% of all adults in the U.S.[12] That same year, more than 1.6 million individuals were in either state or Federal prisons, and nearly 800,000 more were in local jails awaiting trial or serving short sentences, typically less than one year.[12] Minority populations are vastly overrepresented within U.S. correctional facilities, with Black males seven times more likely and Hispanic males more than twice as likely as White males to be incarcerated.[10-11] In 2008, Blacks represented 38% and Hispanics represented 20% of all sentenced prisoners, even though they respectively account for only 12% and 13% of the U.S. population. Female incarceration rates reveal similar racial and ethnic disparities, and Black and Hispanic women constitute the most rapidly increasing demographic group in the correctional population.[10-11,13]

The prevalence of HIV is five times higher in state and Federal correctional systems than in the general population, and the rate of confirmed AIDS cases in U.S. prisons is more than two and a half times greater than among nonincarcerated persons.[14-15] In addition to being a marker for HIV infection, incarceration also is a risk factor for HIV infection, because it disrupts social networks and family relationships and leads to economic vulnerability and poor access to social and risk-reduction services.[16-18]

HIV is a major problem in prisons throughout the world, and IDUs are overrepresented in prison populations. The United Nations Office on Drugs and Crime (UNODC) is the lead UNAIDS agency for HIV/AIDS prevention and care for IDUs in prison. UNODC estimates that, at any given time, more than 10 million people are imprisoned worldwide, and given new and released prisoners, more than 30 million people have contact with prisons every year. UNODC notes the high prevalence of substance abuse problems and drug dependence among prisoners in many countries.[19] A review

of data on HIV and injection drug use in prison in low- and middle-income countries noted that in most countries, data were not collected in a systematic fashion and officials were reluctant to release data on HIV and drug use in prison.[6] Of 152 low- and middle-income countries, 142 had information on imprisonment; information on HIV prevalence in prisons was available for 76 countries. Eighteen countries had an HIV prevalence of greater than 10% in their prison populations. IDUs represented over 10% of prison populations in seven countries: Brazil, Mexico, Nepal, Slovakia, Russia, Ukraine, and Vietnam. HIV prevalence of greater than 10% was reported among IDUs in China (42%), India (80%), Indonesia (56%), Iran (12–63%), Libya (60%), Russia (46%), and Serbia and Montenegro (50%). HIV prevalence among IDUs was also found to vary significantly by site in a given country; in Iran, one site reported 12%, another 63%. Little data were available on the relationship between gender and HIV prevalence and injection drug use. Generally, the limited existing data suggest that HIV prevalence rates are higher for women than for men.

Decades of international data support the effectiveness of harm-reduction programs over punitive drug control policies. A recent review by Vlahov et al. (2010) indicates that drug enforcement expenditures have not prevented an increase in the number of drug users and a decrease in drug prices. Zero tolerance policies used in the "war on drugs" have resulted in severe unintended consequences, such as high incarceration rates, increased stigma of those who need treatment, and large numbers of deaths. The authors state that rapid scale-up of evidence-based harm reduction interventions (e.g., needle exchange programs, methadone and buprenorphine treatment, and identification and treatment of drug use) should be a global public health imperative.[20]

At the January 2010 meeting, Dr. A. Thomas McLellan, Deputy Director of the Office of National Drug Control Policy (ONDCP), indicated that ONDCP plans to focus on populations most in need, including drug-related offenders. Most of these offenders enter the criminal justice system without drug abuse treatment. He noted that the U.S. is working to change drug policy internationally. ONDCP has signaled an end to the "war on drugs" and recognizes that criminal justice alone cannot control illicit drug use. A science-based, public health approach is receiving greater emphasis.

HIV Transmission and Prevention Strategies in Prisons

A recent review of interventions for injection drug users in prison documented that those who inject drugs frequently share injection equipment. In addition, this review listed several studies with evidence for HIV transmission through injection drug use in prison.[21] Recent reports have described high levels of injection drug use and syringe-sharing in prisons in Canada and Thailand.[22-23] Documented cases of HIV transmission in prison are rare in the literature.[6,24] Transmission among prison inmates may be due to unprotected sexual behavior, either consensual or forced; sharing of tattooing equipment; or sharing of drug injection paraphernalia.[6,25] The extent of transmission that occurs in prison may vary greatly from prison to prison and from country to country, but regardless of the extent of transmission behind bars, the burden of infectious diseases is high.[26] In the U.S., transmission in prison represents a small fraction of HIV cases. A study of male inmates in the state of Georgia reported that only about 10% of HIV infections were acquired in prison, and all of these were associated with unprotected sex.[25,27] A study from the state of Rhode Island reported no incident HIV infections among 446 incarcerated males observed for 694 person-years, although transmission of viral hepatitis did occur.[28]

Because of the significant level of risk behavior in prison populations, in 2006, UNODC, the World Health Organization (WHO), and UNAIDS issued "HIV/AIDS Prevention, Care, Treatment and Support in Prison Settings: A Framework for an Effective National Response,"[29] which has the following objectives:

- Providing prisoners with prevention, care, treatment, and support for HIV/AIDS that is equivalent to that available to people in the community outside of prison;
- Preventing the spread of HIV (and other infections) among prisoners, to prison staff, and to the broader community; and
- Promoting an integrated approach to health care within prisons to tackle wider public health issues, both through improvements in health care in general and through improvements in general prison conditions and management.

Strategies that could be employed to reduce the risk of HIV transmission in prison include:

1. Reducing prison populations;
2. Educating prisoners and staff about HIV;
3. Providing opioid substitution therapy (OST);
4. Providing sterile injection equipment;
5. Providing condoms;
6. Providing bleach, if syringe exchange is unacceptable; and
7. Offering HIV testing.

(Adapted from.[6])

The UNAIDS 2008 Report on the global AIDS epidemic reported that one-third of countries have laws, regulations, or policies that present obstacles to effective HIV services for prisoners. The report also noted that only Spain, Switzerland, and the Islamic Republic of Iran offer comprehensive prison-based harm-reduction and treatment services for drug users.[30]

Jurgens et al. reviewed IDU-specific interventions—needle and syringe programs (NSP), bleach, and OST. They argue that these interventions are important in preventing HIV transmission and are not incompatible with the goal of reducing drug use in prison.[21] Bruce and Schleifer describe the ethical and human rights imperatives that should lead governments to offer opioid substitution therapy in prison and detention.[31] A review of OST programs internationally showed that the number of countries or territories that have implemented OST in prison has increased to 29 in 2008 compared with only 5 in 1996; yet 37 countries do not offer OST in prison, although it is available in the community. This is not in keeping with the UNODC 2006 framework.[32]

A 2008 survey in U.S. state and Federal prisons found that fewer than 2,000 prisoners receive OST, even though 9% of Federal prisoners (15,689) and 13% of state prisoners (163,005) had reported regularly using heroin in 2004.[33] The survey found that access to OST in prison in 2008 did not differ from that reported in 2003, but 2008 saw an increase in referral to community-based providers upon release from prison. The survey documented attitudes and practices among correctional medical directors and demonstrated the need to educate prison staff and policymakers about the medical and social benefits of OST. OST in prison and, particularly, upon release to the community, provides the opportunity to break the cycle of addiction, health risks, criminal behavior, and reincarceration.

Opportunity to Implement "Seek, Test, Treat, and Retain" in Corrections Populations

Because HIV infection is overrepresented in corrections populations, intervening in this group has significant potential for affecting the course of the epidemic. In her presentation at the consultation meeting, Dr. Nora Volkow, Director of NIDA, emphasized the public health opportunity of intervening in criminal justice settings with this population of high-risk individuals. Because they are concentrated in criminal justice settings, it is efficient to test them for HIV, provide risk-reduction counseling, and provide highly active antiretroviral therapy (HAART), and to plan for linkages to care upon release while they are still incarcerated. This would decrease the problems inherent in seeking out these hard-to-reach, high-risk individuals in the community.

The U.S. Centers for Disease Control and Prevention (CDC) has promulgated HIV Testing Implementation Guidelines for Correctional Settings (2008)[34] and recommends routine, opt-out testing. Nonetheless, testing policies vary across correctional facilities, and routine HIV testing is not the standard of care in the majority of prisons and jails.[35] In different settings, HIV testing may be made available upon request from the inmate, performed when there is clinical suspicion of infection by a healthcare provider (diagnostic testing), routinely offered upon entrance to the facility and/or upon release, or testing may be mandatory for all inmates or ordered by the court. A study of HIV testing in the North Carolina prison system found that testing varied modestly by prisoner characteristics, but varied greatly by intake prison.[36] Risk-based screening may miss at-risk persons due to inmates' reluctance to report true risk factors; Rosen et al. found only modest associations between inmates' self-reported risk behaviors and infection status.[36] Liddicoat et al. compared the outcomes of a routine HIV testing program in a Massachusetts county prison to a control period during which testing was completed only after inmate or physician request. The rate of HIV testing in the routine testing program increased to 78.2% from 18.0% in the control period. Two inmates were found to be HIV infected—neither had been tested within the prior 3 years.[37]

Jails have high turnover rates and, therefore, have had difficulties implementing HIV testing. The development of rapid testing has created new opportunities for HIV testing within

jails.[35,38] A study from South Carolina demonstrated that lack of HIV screening in correctional facilities (jails, lockups, and detention centers) resulted in missed opportunities to diagnose individuals earlier in the course of their disease and/or to provide prevention education.[39] MacGowan et al. implemented voluntary rapid HIV testing in jails in four states, Florida, Louisiana, upstate New York, and Wisconsin, with the support of state health departments. Of 33,211 individuals voluntarily tested for HIV, 99.9% of inmates were able to receive their rapid test results.[40] Thirty-five percent had never been tested for HIV, and 269 (0.8%) new infections were identified.[40] A jail-based rapid testing program in Rhode Island described by Beckwith et al. successfully delivered rapid test results and prevention counseling to 100% of participants.[41] Two studies of prospective controlled trials of jail testing—one conducted in the only women's jail in Connecticut and the other in a men's jail in New Haven—found that opt-out testing is feasible. More inmates agreed to undergo HIV testing when they were offered testing within 24 hours of incarceration.[42-43]

HIV Treatment in Prison

The administration of highly active antiretroviral therapy (HAART) within correctional facilities is feasible.[44] It has been demonstrated that treatment can result in impressive viral load suppression and increased CD4 counts in HIV-positive prisoners,[45-46] and with appropriate clinical HIV care within corrections, outcomes are comparable to community cohorts.[47] Nonetheless, standardized care for HIV within prisons is not the norm. A study in Texas found that only one-third of inmates who met the criteria for initiation of HAART were actually on therapy.[48] An analysis of expenditures for antiretroviral drugs by correctional facilities suggested that approximately one-third of HIV-infected inmates were receiving HAART.[49] Stigmatization and misunderstanding of HIV/AIDS among correctional staff and service providers also can be a significant barrier to delivering HIV-related services.[50] Moreover, in-prison service providers find it difficult to maintain confidentiality with regard to inmates' HIV status because of the prison setting and described lack of internal coordination between service providers.[50] Allowing prisoners to keep medications on their person rather than using "pill lines," where prisoners retrieve medications from a central facility, may increase the acceptability of treatment and alleviate concerns about confidentiality and stigma.[44]

Linkages to Care upon Community Reentry

The post-release period is critical for maintaining viral suppression among prisoners on HAART. Although prisoners may receive appropriate HIV treatment and care during their incarceration, many have limited or no access to health services in the community.[47,51] Prisoners receiving HAART who remained incarcerated had better virological outcomes than did those on HAART who were released and subsequently reincarcerated because of the increased likelihood of treatment interruptions among those transitioning between corrections and the community.[47,52]

- Even when effective HIV treatment is initiated in prison, there are difficulties in maintaining treatment upon release.[53] A study from Texas found that only 5.4% of prisoners leaving corrections filled antiretroviral prescriptions in time to avoid an interruption in care, and only 30% had filled prescriptions 60 days after release.[53] A study of those released and reincarcerated in San Francisco jails found that lapses in HAART treatment were associated with homelessness, marijuana use, injection drug use, and a lack of community medical care.[54] Another study on a cohort of prisoners going in and out of jail in San Francisco reported that the majority of inmates interrupted HAART after release from jail (76%), and only 15% stayed on HAART continuously.[55] Prisoners face momentous challenges upon release to the community. In the 2 weeks following release, there is a 12.8 times increased risk for all-cause mortality; the leading cause of death is overdose.[56] Relapse to addiction is frequent, and untreated mental illness, homelessness, and poverty all act as significant barriers to care. A study that instituted pharmacological treatment of addiction (buprenorphine/naloxone) in HIV-positive prisoners prior to release demonstrated sustained reductions in viral load and CD4 counts for the 12-week follow-up period.[57] Reentry is a critical time to link individuals to community-based HIV care and other health and social services that will ensure continuity of treatment and address the major stressors and risk behaviors associated with community transition.

Case management interventions have been developed to improve linkage to care for HIV-infected prisoners. Particularly effective are collaborations between community-based organizations and correctional facilities, which involve service provision within the correctional setting and follow-up care post-release.[58] In Rhode Island, Project Bridge, an 18-month intensive case management program, reported that

75% of those released received specialty medical care from community providers, and 100% received HIV-related medical services.[59] A HRSA-funded Special Project of National Significance, "Enhancing Linkages to HIV Primary Care in Jail Settings," which is being conducted in 10 sites across the U.S. is now evaluating integrated case management models of linkage in jail facilities.[60] Formative research has been conducted to adapt an evidence-based intervention (EBI), the "Holistic Health Recovery Program," that integrates HIV risk reduction and HAART adherence to prisoners transitioning to the community.[61]

While case management for HIV-positive inmates returning to the community can promote sustained linkage to HIV treatment and care, it also can have a positive impact on secondary transmission. However, case management alone has been shown to facilitate mostly short-term behavioral risk reduction and tends to have a less significant impact on sexual risk behaviors.[51,62] Approaches that integrate case management with targeted risk-reduction programs may be more capable of promoting sustained risk reduction in this population.

TB and HCV Infection in Criminal Justice Settings

Hepatitis C (HCV) and tuberculosis (TB) infections are overrepresented in criminal justice populations[26,63] and frequently occur as co-infections with HIV. A discussion of HCV and TB co-infection in drug-using populations is included in Chapter 3; the following discussion focuses on co-infections in criminal justice systems.

Tuberculosis prevalence in criminal justice systems has been reported to be up to 100 times greater than in the general population; criminal justice settings may account for up to 25% of a country's TB cases.[63] Multidrug-resistant (MDR) TB also is highly prevalent in these populations. In fact, a modeling study that did a cross-country analysis of Eastern European and Central Asian countries found that high incarceration rates were associated with increased TB incidence and increases in MDR TB. Increases in incarceration of HIV-infected IDUs account for an important part of the adverse effects of incarceration on TB.[64] WHO has developed a manual for program managers called " Tuberculosis Control in Prisons."[65] The Tuberculosis Coalition for Technical Assistance has developed "Guidelines for the Control of Tuberculosis in Prisons."[66] The U.S. CDC has published "Prevention and Control of Tuberculosis in Correctional and Detention Facilities: Recommendations from CDC,"[67] and in 2010, the U.S. Federal Bureau of Prisons revised its Clinical Practice Guidelines on "Management of Tuberculosis."[68] The WHO Europe Health in Prison Project has explored some of the barriers to implementation of effective TB control in prisons.[69] In the U.S., a study of TB prevention and control in 20 large jail systems indicated that improvements were needed, especially information on HIV status.[70]

HCV infection also is prevalent in criminal justice settings, particularly among injection drug users.[26,71-75] Incident hepatitis infection in prison linked to continued injection drug use and sharing of injection equipment has been reported.[76] Among inmates with HIV infection, HCV co-infection is common.[71,77-78] Given high rates of co-infection, it has been suggested that all HIV-positive inmates be tested for HCV.[78] Use of risk-based HCV testing, specifically testing of those who self-report injection drug use, is likely to miss significant numbers of infections.[79] Prisons provide an opportunity to treat chronic HCV among individuals who might otherwise have limited access to therapy.[73,80] In the U.S., provision of services for HCV in correctional settings would be improved by the formation of partnerships between correctional and public health agencies.[81-82] The U.S. CDC published recommendations for "Prevention and Control of Infections with Hepatitis in Correctional Settings,"[83] and the U.S. Federal Bureau of Prisons has developed "Guidelines for the Prevention and Treatment of Hepatitis C and Cirrhosis."[84]

Conclusion and Recommendations

Prisoners bear a disproportionate burden of HIV, due in large part to the overrepresentation of the addicted, the mentally ill, and minority populations within corrections settings. HIV testing, treatment, and discharge planning are all key components of meaningful HIV care in these settings. While successful treatment during incarceration has been well documented, much of the benefit of virological suppression is lost upon release when individuals face often insurmountable barriers to care. Successful discharge planning and intensive case management during the transition from corrections to the community is critical to ensure adherence to HAART and linkage to care. Particular attention needs to be paid to treating mental illness and offering opioid substitution therapy and addictions treatment while incarcerated and addressing practical issues, such as housing, employment, and food on release. Although much progress has been made in the science of addiction treatment, there is still the need to educate prison staff and policymakers about the medical and social benefits of treatment, particularly OST.

In his presentation, Dr. Josiah Rich of the Miriam Hospital and Brown University Medical School identified the following goals and challenges:

- To maximize HIV testing of prisoners;
- To optimize quality care for HIV and co-occurring disorders and ensure confidentiality;
- To optimize reentry and linkages to comprehensive care and services;
- To reduce recidivism; and
- To implement primary and secondary HIV prevention.

These recommendations and priorities were endorsed by the criminal justice breakout group. Additional criminal justice recommendations were made by the human rights and vulnerable populations breakout group, the drug abuse treatment as HIV prevention breakout, and the HIV prevention implementation breakout. All recommendations are found in Appendix A.

The need for more research on the implementation of seek, test, treat, and retain in criminal justice settings was endorsed by Dr. Anthony Fauci, Director of NIAID, in his presentation. Dr. Fauci noted that NIAID and the National Institute of Mental Health (NIMH) had joined a NIDA-initiated $10.6 million Request for Applications (RFA) that encouraged researchers to develop, implement, and evaluate strategies to increase HIV testing and the provision of HAART to HIV-seropositive individuals in the criminal justice system, with a particular focus on continuity of HAART during and after community reentry following incarceration. It is anticipated that 7-10 new awards will be made in September, 2010.

References

[1] Chandler, R.K., Fletcher, B.W., & Volkow, N.D. Treating drug abuse and addiction in the criminal justice system: Improving public health and safety. *JAMA: Journal of the American Medical Association* 301, 183–190, 2009.

[2] DeBeck, K., Kerr, T., Li, K., Milloy, M.J., Montaner, J., & Wood, E. Incarceration and drug use patterns among a cohort of injection drug users. *Addiction* 104, 69–76, 2009.

[3] Reuter, P. Ten years after the United Nations General Assembly Special Session (UNGASS): Assessing drug problems, policies and reform proposals. *Addiction* 104, 510–517, 2009.

[4] HIV in prisons. *Lancet Infectious Diseases* 7, 1, 2007.

[5] Belenko, S. & Peugh, J. Estimating drug treatment needs among state prison inmates. *Drug and Alcohol Dependence* 77, 269–281, 2005.

[6] Dolan, K., Kite, B., Black, E., Aceijas, C., & Stimson, G.V. HIV in prison in low-income and middle-income countries. *Lancet Infectious Diseases* 7, 32–41, 2007.

[7] Mumola, C. & Karberg, J. Drug use and dependence, state and federal prisoners, 2006. (2006). http://bjs.ojp.usdoj.gov/index.cfm?ty=pbdetail&iid=778.

[8] Maru, D.S., Basu, S., & Altice, F.L. HIV control efforts should directly address incarceration. *Lancet Infectious Diseases* 7, 568–569, 2007.

[9] Wood, E., Werb, D., Marshall, B.D., Montaner, J.S., & Kerr, T. The war on drugs: A devastating public-policy disaster. *Lancet* 373, 989–990, 2009.

[10] Minton, T. & Sabol, W. Jail Inmates at Midyear 2008. Washington, DC: U.S. Department of Justice, Bureau of Justice Statistics, 2009. http://bjs.ojp.usdoj.gov/index.cfm?ty=pbdetail&iid=1004

[11] Sabol, W., West, H., & Cooper, M. Prisoners in 2008. Washington, DC: U.S. Department of Justice, Bureau of Justice Statistics, 2009. http://bjs.ojp.usdoj.gov/index.cfm?ty=pbdetail&iid=1763

[12] Glaze, L. & Bonczar, T. Probation and Parole in the United States 2008. Washington, DC: U.S. Department of Justice, Bureau of Justice Statistics, 2009. http://bjs.ojp.usdoj.gov/index.cfm?ty=pbdetail&iid=1764.

[13] Braithwaite, R.L., Treadwell, H.M. & Arriola, K.R. Health disparities and incarcerated women: A population ignored. *American Journal of Public Health* 98, S173–175, 2008.

[14] Spaulding, A., Stephenson, B., Macalino, G., Ruby, W., Clarke, J.G., & Flanigan, T.P. Human immunodeficiency virus in correctional facilities: A review. *Clinical Infectious Diseases* 35, 305–312, 2002.

[15] Maruschak, L. HIV in Prisons, 2006. Washington, DC: U.S. Department of Justice, Bureau of Justice Statistics, 2008. http://bjs.ojp.usdoj.gov/index.cfm?ty=pbdetail&iid=952.

[16] Blankenship, K.M., Smoyer, A.B., Bray, S.J., & Mattocks, K. Black-white disparities in HIV/AIDS: The role of drug policy and the corrections system. *Journal of Health Care for the Poor and Underserved* 16, 140–156, 2005.

[17] Khan, M.R., Doherty, I.A., Schoenbach, V.J., Taylor, E.M., Epperson, M.W., & Adimora, A.A. Incarceration and high-risk sex partnerships among men in the United States. *Journal of Urban Health* 86, 584–601, 2009.

[18] Moore, L.D. & Elkavich, A. Who's using and who's doing time: Incarceration, the war on drugs, and public health. *American Journal of Public Health* 98, 782–786, 2008.

[19] UNODC. UNODC, Prison Settings. http://www.unodc.org/unodc/en/hiv-aids/prison-settings.html?ref=menuside

[20] Vlahov, D., Robertson, A.M., & Strathdee, S.A. Prevention of HIV infection among injection drug users in resource-limited settings. *Clinical Infectious Diseases* 50 (Suppl 3), S114–121, 2010.

[21] Jurgens, R., Ball, A., & Verster, A. Interventions to reduce HIV transmission related to injecting drug use in prison. *Lancet Infectious Diseases* 9, 57–66, 2009.

[22] Werb, D., Kerr, T., Small, W., Li, K., Montaner, J., & Wood, E. HIV risks associated with incarceration among injection drug users: Implications for prison-based public health strategies. *Journal of Public Health* (Oxf) 30, 126–132, 2008.

[23] Hayashi, K., Milloy, M.J., Fairbairn, N., Kaplan, K., Suwannawong, P., Lai, C., Wood, E., & Kerr, T. Incarceration experiences among a community-recruited sample of injection drug users in Bangkok, Thailand. *BMC Public Health* 9, 492, 2009.

[24] Krebs, C.P. & Simmons, M. Intraprison HIV transmission: An assessment of whether it occurs, how it occurs, and who is at risk. *AIDS Education and Prevention* 14, 53–64, 2002.

[25] Centers for Disease Control and Prevention (CDC). HIV transmission among male inmates in a state prison system, Georgia, 1992–2005. *MMWR Morbidity and Mortality Weekly Report* 55, 421–426, 2006.

[26] Hammett, T.M. HIV/AIDS and other infectious diseases among correctional inmates: Transmission, burden, and an appropriate response. *American Journal of Public Health* 96, 974–978, 2006.

[27] Jafa, K., McElroy, P., Fitzpatrick, L., Borkowf, C.B., Macgowan, R., Margolis, A., Robbins, K., Youngpairoj, A.S., Stratford, D., Greenberg, A., Taussig, J., Shouse, R.L., Lamarre, M., McLellan-Lemal, E., Heneine, W., & Sullivan, P.S. HIV transmission in a state prison system, 1988–2005. *PLoS One* 4, e5416, 2009.

[28] Macalino, G.E., Vlahov, D., Sanford-Colby, S., Patel, S., Sabin, K., Salas, C., & Rich, J.D. Prevalence and incidence of HIV, hepatitis B virus, and hepatitis C virus infections among males in Rhode Island prisons. *American Journal of Public Health* 94, 1218–1223, 2004.

[29] UNODC. HIV/AIDS Prevention, Care, Treatment and Support in Prison Settings: A Framework for an Effective National Response, 2006. http://www.unodc.org/unodc/en/hiv-aids/publications.html?ref=menuside.

[30] UNAIDS. The UNAIDS 2008 Report on the global AIDS epidemic. 2008. http://www.unaids.org/en/KnowledgeCentre/HIVData/GlobalReport/2008/.

[31] Bruce, R.D. & Schleifer, R.A. Ethical and human rights imperatives to ensure medication-assisted treatment for opioid dependence in prisons and pre-trial detention. *International Journal of Drug Policy* 19, 17–23, 2008.

[32] Larney, S. & Dolan, K. A literature review of international implementation of opioid substitution treatment in prisons: Equivalence of care? *European Addiction Research* 15, 107–112, 2009.

[33] Nunn, A., Zaller, N., Dickman, S., Trimbur, C., Nijhawan, A., & Rich, J.D. Methadone and buprenorphine prescribing and referral practices in US prison systems: Results from a nationwide survey. *Drug and Alcohol Dependence* 105, 83–88, 2009.

[34] Centers for Disease Control and Prevention (CDC). HIV Testing Implementation Guidelines for Correctional Settings. Atlanta, GA: CDC, 2008. http://www.cdc.gov/hiv/topics/testing/resources/guidelines/correctional-settings/index.htm].

[35] Zaller, N., Dawalt, M., Beckwith, C., Rich, J.D., & Flanigan, T.P. Routine HIV testing in US prisons. *Lancet Infectious Diseases* 7, 440–441, 2007.

[36] Rosen, D.L., Schoenbach, V.J., Wohl, D.A., White, B.L., Stewart, P.W., & Golin, C. E. An evaluation of HIV testing among inmates in the North Carolina prison system. *American Journal of Public Health* 99 (Suppl 2), S452–459, 2009.

[37] Liddicoat, R.V., Zheng, H., Internicola, J., Werner, B.G., Kazianis, A., Golan, Y., Rubinstein, E.P., Freedberg, K.A., & Walensky, R.P. Implementing a routine, voluntary HIV testing program in a Massachusetts county prison. *Journal of Urban Health* 83, 1127–1131, 2006.

[38] Kavasery, R. & Altice, F.L. Observations on implementing routine HIV testing in jails. *AIDS Patient Care STDS* 21, 715–716, 2007; author reply 717, 2007.

[39] Duffus, W.A., Youmans, E., Stephens, T., Gibons, J.J. Albrecht, H., & Potter, R. H. Missed opportunities for early HIV diagnosis in correctional facilities. *AIDS Patient Care STDS* 23, 1025–1032, 2009.

[40] Macgowan, R., l. Margolis, A., Richardson-Moore, A., Wang, T., Lalota, M., French, P.T., Stodola, J., McKeever, J., Carrel, J., Mullins, J., Llanas, M., Griffiths, S.D., & the Rapid Testing in Corrections (RTIC) Team. Voluntary rapid human immunodeficiency virus (HIV) testing in jails. *Sexually Transmitted Diseases* 36, S9–13, 2009.

[41] Beckwith, C.G., Atunah-Jay, S., Cohen, J., Macalino, G., Poshkus, M., Rich, J.D.., Flanigan, T.P., & Lally, M.A. Feasibility and acceptability of rapid HIV testing in jail. *AIDS Patient Care STDS* 21, 41–47, 2007.

[42] Kavasery, R., Maru, D.S., Cornman-Homonoff, J., Sylla, L.N., Smith, D., & Altice, F.L. Routine opt-out HIV testing strategies in a female jail setting: A prospective controlled trial. *PLoS One* 4, e7648, 2009.

[43] Kavasery, R., Maru, D.S., Sylla, L.N., Smith, D., & Altice, F.L. A prospective controlled trial of routine opt-out HIV testing in a men's jail. *PLoS One* 4, e8056, 2009.

[44] Pontali, E. Antiretroviral treatment in correctional facilities. *HIV Clinical Trials* 6, 25–37, 2005.

[45] Springer, S.A. & Altice, F.L. Managing HIV/AIDS in correctional settings. *Current HIV/AIDS Report* 2, 165–170, 2005.

[46] Springer, S.A., Friedland, G.H., Doros, G., Pesanti, E., & Altice, F.L. Antiretroviral treatment regimen outcomes among HIV-infected prisoners. *HIV Clinical Trials* 8, 205–212, 2007.

[47] Springer, S.A., Pesanti, E., Hodges, J., Macura, T., Doros, G., & Altice, F.L. Effectiveness of antiretroviral therapy among HIV-infected prisoners: Reincarceration and the lack of sustained benefit after release to the community. *Clinical Infectious Diseases* 38, 1754–1760, 2004.

[48] Baillargeon, J., Borucki, M.J., Zepeda, S., Jenson, H.B., & Leach, C.T. Antiretroviral prescribing patterns in the Texas prison system. *Clinical Infectious Diseases* 31, 1476–1481, 2000.

[49] Zaller, N., Thurmond, P., & Rich, J.D. Limited spending: An analysis of correctional expenditures on antiretrovirals for HIV-infected prisoners. *Public Health Report* 122, 49–54, 2007.

[50] Grinstead, O., Seal, D.W., Wolitski, R., Flanigan, T., Fitzgerald, C., Nealey-Moore, J., Askew, J., & the Project START Study Group. HIV and STD testing in prisons: Perspectives of in-prison service providers. *AIDS Education and Prevention* 15, 547–560, 2003.

[51] White, M.C., Tulsky, J.P., Estes, M., Jamison, R., & Long, H.L. Health and health behaviors in HIV-infected jail inmates, 1999 and 2005. *AIDS Patient Care STDS* 22, 221–231, 2008.

[52] Stephenson, B.L., Wohl, D.A., Golin, C.E., Tien, H.C., Stewart, P., & Kaplan, A.H. Effect of release from prison and re-incarceration on the viral loads of HIV-infected individuals. *Public Health Report* 120, 84–88, 2005.

[53] Baillargeon, J., Giordano, T.P., Rich, J.D., Wu, Z.H., Wells, K., Pollock, B.H., & Paar, D.P. Accessing antiretroviral therapy following release from prison. *JAMA: Journal of the American Medical Association* 301, 848–857, 2009.

[54] Clements-Nolle, K., Marx, R., Pendo, M., Loughran, E., Estes, M., & Katz, M. Highly active antiretroviral therapy use and HIV transmission risk behaviors among individuals who are HIV infected and were recently released from jail. *American Journal of Public Health* 98, 661–666, 2008.

[55] Pai, N.P., Estes, M., Moodie, E.E., Reingold, A.L., & Tulsky, J.P. The impact of antiretroviral therapy in a cohort of HIV infected patients going in and out of the San Francisco county jail. *PLoS One* 4, e7115, 2009.

[56] Binswanger, I.A., Stern, M.F., Deyo, R.A., Heagerty, P.J., Cheadle, A., Elmore, J.G., & Koepsell, T.D. Release from prison: A high-risk of death for former inmates. *New England Journal of Medicine* 356, 157–165, 2007.

[57] Springer, S.A., Chen, S., & Altice, F.L. Improved HIV and Substance Abuse Treatment Outcomes for Released HIV-Infected Prisoners: The Impact of Buprenorphine Treatment. *Journal of Urban Health* (epub ahead of print, February 2010).

[58] Klein, S.J., O'Connell, D.A., Devore, B.S., Wright, L.N., & Birkhead, G.S. Building an HIV continuum for inmates: New York State's criminal justice initiative. *AIDS Education and Prevention* 14, 114–123, 2002.

[59] Rich, J.D., Holmes, L., Salas, C., Macalino, G., Davis, D., Ryczek, J., & Flanigan, T. Successful linkage of medical care and community services for HIV-positive offenders being released from prison. *Journal of Urban Health* 78, 279–289, 2001.

[60] Spaulding, A.C., Arriola, K.R., Hammett, T., Kennedy, S., & Tinsley, M. Rapid HIV testing in rapidly released detainees: Next steps. *Sexually Transmitted Diseases* 36, S34–36, 2009.

[61] Copenhaver, M., Chowdhury, S., & Altice, F.L. Adaptation of an evidence-based intervention targeting HIV-infected prisoners transitioning to the community: The process and outcome of formative research for the Positive Living Using Safety (PLUS) intervention. *AIDS Patient Care STDS* 23, 277–287, 2009.

[62] Needels, K., James-Burdumy, S., & Burghardt, J. Community case management for former jail inmates: Its impacts on rearrest, drug use, and HIV risk. *Journal of Urban Health* 82, 420–433, 2005.

[63] World Health Organization (WHO). Tuberculosis in Prisons. http://www.who.int/tb/challenges/prisons/story_1/en/index.html

[64] Stuckler, D., Basu, S., McKee, M., & King, L. Mass incarceration can explain population increases in TB and multidrug-resistant TB in European and central Asian countries. Proceedings of the National Academy of Science USA 105, 13280–13285, 2008.

[65] World Health Organization (WHO). Tuberculosis Control in Prisons. http://www.who.int/tb/publications/prisons_tb_control_manual/en/index.html

[66] Tuberculosis Coalition for Technical Assistance. Guidelines for Control of Tuberculosis in Prisons, 2009. http://www.tbcta.org/Library/#16

[67] Centers for Disease Control and Prevention (CDC). Prevention and control of tuberculosis in correctional and detention facilities: Recommendations from CDC. Endorsed by the Advisory Council for the Elimination of Tuberculosis, the National Commission on Correctional Health Care, and the American Correctional Association. *MMWR Recommendations and Reports* 55, 1–44, 2006.

[68] U.S. Federal Bureau of Prisons. Clinical Practice Guidelines on "Management of Tuberculosis." 2010. http://www.bop.gov/news/medresources.jsp.

[69] Moller, L., Gatherer, A., & Dara, M. Barriers to implementation of effective tuberculosis control in prisons. Public Health 123, 419–421, 2009.

[70] Roberts, C.A., Lobato, M.N., Bazerman, L.B., Kling, R., Reichard, A.A., & Hammett, T.M. Tuberculosis prevention and control in large jails: A challenge to tuberculosis elimination. *American Journal of Preventive Medicine* 30, 125–130, 2006.

[71] Weinbaum, C.M., Sabin, K.M., & Santibanez, S.S. Hepatitis B, hepatitis C, and HIV in correctional populations: A review of epidemiology and prevention. *AIDS* 19 (Suppl) 3, S41–46, 2005.

[72] Adjei, A.A., Armah, H.B., Gbagbo, F., Ampofo, W.K., Boamah, I., Adu-Gyamfi, C., Asare, I., Hesse, I.F., & Mensah, G. Correlates of HIV, HBV, HCV and syphilis infections among prison inmates and officers in Ghana: A national multicenter study. *BMC Infectious Diseases* 8, 33, 2008.

[73] Strock, P., Mossong, J., Hawotte, K., & Arendt, V. Access to treatment of hepatitis C in prison inmates. *Digestive Diseases and Sciences* 54, 1325–1330, 2009.

[74] Verneuil, L., Vidal, J.S., Ze Bekolo, R., Vabret, A., Petijean, L., Leclercq, R., & Leroy, Dl. Prevalence and risk factors of the whole spectrum of sexually transmitted diseases in male incoming prisoners in France. *European Journal of Clinical Microbiology of Infectious Diseases* 28, 409–413, 2009.

[75] Vescio, M.F., Longo, B., Babudieri, S., Starnini, G., Carbonara, S., Rezza, G., & Monarca, Rl. Correlates of hepatitis C virus seropositivity in prison inmates: A meta-analysis. *Journal of Epidemiology and Community Health* 62, 305–313, 2008.

[76] Dolan, K., Teutsch, S., Scheuer, N., Levy, M., Rawlinson, W., Kaldor, J., Lloyd, A. & Haber, P. Incidence and risk for acute hepatitis C infection during imprisonment in Australia. *European Journal of Epidemiology* 25, 143–148, 2010.

[77] Hennessey, K.A., Kim, A.A., Griffin, V., Collins, N.T., Weinbaum, C.M., & Sabin, K. Prevalence of infection with hepatitis B and C viruses and co-infection with HIV in three jails: A case for viral hepatitis prevention in jails in the United States. *Journal of Urban Health* 86, 93–105, 2009.

[78] Pontali, E. & Ferrari, F. Prevalence of Hepatitis B virus and/or Hepatitis C virus co-infections in prisoners infected with the Human Immunodeficiency Virus. *International Journal of Prison Health* 4, 77–82, 2008.

[79] Macalino, G.E., Dhawan, D., & Rich, J.D. A missed opportunity: Hepatitis C screening of prisoners. *American Journal of Public Health* 95, 1739–1740, 2005.

[80] Maru, D.S., Bruce, R.D., Basu, S., & Altice, F.L. Clinical outcomes of hepatitis C treatment in a prison setting: Feasibility and effectiveness for challenging treatment populations. *Clinical Infectious Diseases* 47, 952–961, 2008.

[81] Chow, J.M., Joesoef, M.R., Kent, C., Weinstock, H., & Fenton, K. Responding to the burden of STD, HIV, and viral hepatitis in correctional populations through program collaboration and integration. *Sexually Transmitted Diseases* 36, S1–2, 2009.

[82] Spaulding, A.C., Weinbaum, C.M., Lau, D.T., Sterling, R., Seeff, L.B., Margolis, H.S., & Hoofnagle, J. H. A framework for management of hepatitis C in prisons. *Annals of Internal Medicine* 144, 762–769, 2006.

[83] Weinbaum, C., Lyerla, R., & Margolis, H.S. Prevention and control of infections with hepatitis viruses in correctional settings. Centers for Disease Control and Prevention. *MMWR Recommendations and Reports* 52, 1–36; quiz CE31–34 (2003).

[84] U.S. Federal Bureau of Prisons. Guidelines for the Prevention and Treatment of Hepatitis C and Cirrhosis. http://www.bop.gov/news/medresources.jsp.

Chapter 6. Human Rights and At-Risk and Vulnerable Populations

In his presentation at the consultation meeting, Mr. Daniel Wolfe of the Open Society Institute, International Harm Reduction Development Program, addressed human rights and HIV prevention, treatment, and care. He noted that researchers and health providers who work with injection drug users (IDUs) have long addressed the need for both service provision and the protection of human rights. He noted that human rights advocates have typically drawn from a different set of normative standards than health providers: They are more likely to cite the Universal Declaration of Human Rights or other international human rights conventions[1] than a guideline from the World Health Organization (WHO). However, human rights advocates increasingly have found common cause with those working to reduce the adverse health impacts of illicit drug use.[2-4] Core principles of human rights include security of the person; self-determination; the right to privacy; and freedom from cruel, inhuman, or degrading treatment.[5-6] These principles overlap with elements of effective health programming for those in substance abuse treatment, where client trust and the therapeutic alliance are critical.[7-8]

However, the limits of the alliance between public health and human rights are regularly tested. In fact, service providers, human rights advocates, policymakers, law enforcement personnel, and public health officials often have disparate views as they seek to reconcile the goals of protecting individual liberties, the public health, and the safety of all citizens. Human rights proponents themselves differ about attainable standards and the proper allocation of resources.[9-10] In the case of HIV, national commitments to universal access to prevention and treatment, and the recognition that IDUs and other drug users do not forfeit their entitlement to health services or human dignity, offer a clear point of convergence for advocates for health and rights. The focus on the protection of vulnerable populations in human rights treaties is particularly resonant with HIV prevention and treatment professionals.

A review by Stemple describes the history of the alliance between public health and human rights in the context of HIV/AIDS, discusses recent developments in human rights and HIV/AIDS, and makes recommendations for enhancing human rights in the context of HIV/AIDS.[11] The review notes that despite the fact that health and rights can strengthen each other, many health professionals are unschooled about human rights and have misconceptions. Stemple suggests that human rights practitioners should evaluate their interventions using standards common in the social sciences in order to demonstrate that rights-based interventions can have positive health outcomes. A similar approach proposes using health and human rights indicators to show progress, to highlight disparities within countries and globally, and to determine whether policies and programs that are most effective in terms of health also achieve the greatest level of compliance with human rights.[12]

This chapter focuses on the conditions of several populations that tend to have a higher prevalence of HIV infection than that of the general population and whose human rights must be safeguarded: women in the developing world, sex workers, and men who have sex with men. In many countries, these populations are among the most marginalized and discriminated against in society. At the same time, the resources devoted to HIV prevention, treatment, and care for these populations are not proportional to their HIV prevalence—a serious mismanagement of resources and a failure to respect fundamental human rights.

Two populations at high risk for HIV—injection and other drug users and criminal justice populations—are addressed in separate chapters because of the high prevalence of disease and acute barriers involved in prevention, treatment, and care for their complex needs. Because of the illegality of drug use and the stigma associated with it, injection drug users often are estranged from the health care system and perceive little reason to seek medical services. The need for comprehensive services that address both HIV and drug abuse was the primary focus of the consultation meeting and is examined in depth in chapters 3 and 4 and throughout this report. Conditions in most prisons make them extremely high-risk environments for HIV transmission, leading them to be called "incubators" of HIV infection, as well as of hepatitis C

and tuberculosis.[13] The needs of the criminal justice population are described in chapter 5.

This chapter describes of the ways in which stigma and discrimination underlie and perpetuate the vulnerability of at-risk populations. It examines gender inequality and the factors that undermine women's autonomy, particularly in the developing world. This is followed by a discussion of sex work, drug use, and HIV. Finally, the chapter addresses the challenges of men who have sex with men. The theme of protection of human rights in all programs that provide prevention, treatment, and care for these populations is the unifying thread of this chapter.

Stigma, Discrimination, and Vulnerability to HIV

Stigma, discrimination, and social marginalization are causes of HIV risk and vulnerability, and consequences of being HIV positive. Stigmatizing attitudes to HIV and those most at risk of HIV infection derive from two principal sources.[14] The first is fear of contagion, which has been a source of disease-related stigma throughout the ages. The second is negative, value-based assumptions about people living with HIV, which fuels prejudice and discrimination.[15] In some cases, discrimination against people living with HIV is institutionalized in national and local laws. According to the European AIDS Treatment Group, many countries restrict the entry, residence, and stay of people who are HIV positive.[16]

HIV-related stigma and discrimination undermine HIV prevention efforts by making people reluctant to be tested, and reluctant to seek out information about how to protect themselves from infection. Fear of stigma and discrimination also makes people living with HIV less likely to seek care and treatment, adhere to treatment, and disclose their HIV status to their sexual partners.[17]

Laws can protect people living with HIV from discrimination or can increase discrimination against them. For example, broadly applying the criminal law to HIV transmission sends the message that people living with HIV are potential criminals.[14] The law also can protect other groups (e.g., men who have sex with men, drug users, or sex workers) from human rights violations, particularly violence, discrimination, and lack of due process. However, when the activities of such groups are criminalized, the law and its enforcement can become a major barrier to access and uptake of HIV prevention, treatment, care, and support.[14] Institutionalized discrimination also is reflected in acts of omission, such as when the level of HIV resources directed to these populations are not commensurate with their needs or local epidemiology, or when HIV surveillance systems fail to track such groups.

Effective Interventions. Over the past few years, the harmful effects of stigma and discrimination have become even more clearly understood, and a growing number of institutions and organizations have focused greater attention on these effects.[14] A number of successful approaches and strategies have emerged. They include:

- *Preventing HIV-based discrimination.* Legal protections against HIV discrimination are an essential prerequisite for a sound national HIV response.[18]
- *Promoting HIV knowledge and compassion.* Successful programs often include empowerment of people living with HIV, education about HIV, and activities that foster inter-

HIV Risk and Vulnerability

According to UNAIDS, risk is defined as the probability or likelihood that a person may become infected with HIV. Certain behaviors create, increase, and perpetuate risk. Examples include unprotected sex with a partner whose HIV status is unknown, multiple sexual partnerships involving unprotected sex, and injection drug use with contaminated needles and syringes.

Vulnerability results from a range of factors outside the control of the individual that reduce the ability of individuals and communities to avoid HIV risk. These factors may include: (1) lack of knowledge and skills required to protect oneself and others; (2) factors pertaining to the quality and coverage of services (e.g., inaccessibility of service due to distance, cost or other factors); and (3) societal factors such as human rights violations, or social and cultural norms. These norms can include practices, beliefs, and laws that stigmatize and disempower certain populations, limiting their ability to access or use HIV prevention, treatment, care, and support services and commodities. These factors, alone or in combination, may create or exacerbate individual and collective vulnerability to HIV.[14]

action between people living with HIV and key audiences, including policymakers and high-profile celebrities.[14]

- *Increasing visibility of people living with HIV.* Silence, fear, and shame enable HIV stigma and discrimination to flourish. Between 1996 and 2007, the Network of Zambian People Living with AIDS (NZP+) grew from 28 members to more than 50,000. Through more than 3,000 self-help groups, NZP+ mobilizes its members to combat HIV stigma and to demand better access to high-quality services.[14]

- *Scaling up treatment.* Public investment in antiretroviral therapy (ART) helps mitigate HIV stigma by underscoring the value attached to the lives and well-being of people living with HIV.[14] A longitudinal study in Mombasa, Kenya, found that individuals on antiretroviral drugs had lower levels of internalized stigma 12 months after starting therapy and were more likely to disclose their HIV infection to family members.

- *Prohibiting discrimination against populations most at risk.* The reach of HIV prevention programs for populations most at risk is generally better in countries with non-discrimination laws in place than countries without such laws.[14]

- *Empowering the community among populations most at risk.* Access to social support—sometimes referred to as "social capital"—is vital to reducing vulnerability of marginalized or disempowered groups.[14] In nearly all countries where the HIV epidemic has been reversed, grassroots community mobilization was at the heart of the national HIV response.[19]

Gender Inequality

The many and varied links between gender inequality and increased vulnerability to HIV infection among women and adolescent girls have been well documented.[20] Cultural or social norms often restrict women's access to basic information about sexual and reproductive health. Even if women have access to information and commodities (e.g., condoms), gender norms that prescribe an unequal and more passive role for women in sexual decision-making undermine women's autonomy, expose many to sexual coercion, and prevent them from insisting on abstinence or condom use with their male partners.

Traditional expectations related to masculinity and male sexual behavior also increase the risk of infection among men and boys.[14] Typical male roles that call for men and boys to be tough, aggressive, sexually dominant, and risk-taking often are associated with behaviors that increase men's risk of HIV infection. Such behaviors include a high number of sexual partners, use of drugs or alcohol, and refusal to seek medical care for sexually transmitted infections. The mutually harmful nature of some gender norms underscores the importance of involving men and boys in any effort toward change.

Grieg and colleagues discuss gender and HIV/AIDS and interventions at multiple levels—individual and community as well as national, regional, and global—that are necessary to move forward in addressing the gender dimensions of HIV/AIDS.[21]

Effective Interventions. A growing number of strategies can reduce gender inequality and change harmful gender norms.[14] They include:

- *Education.* Schooling offers an excellent means of reducing girls' HIV risk and vulnerability. Girls who complete primary education are more than twice as likely to use condoms, while girls who finish secondary education are between four and seven times more likely to use condoms, and are less likely to be infected with HIV.

- *Multi-component efforts to change harmful gender norms.* A wide array of promising programs have been developed to help communities develop equitable gender norms.[14] Programs that aimed to transform gender roles through critical reflection, role play, and other interactions were most likely to be effective in producing changes in the targeted attitudes and behaviors.

- *Reduction in gender-based violence.* Widespread violence against women not only represents a global human rights crisis, but also contributes to women's vulnerability to HIV.14 Between 40% and 60% of women surveyed in Bangladesh, Ethiopia, Peru, Samoa, Thailand, and the United Republic of Tanzania said they had been physically and/or sexually abused by their intimate partners.[22] International experience has shown that rates of violence can be lowered. However, 29% of national governments report that they lack laws or policies to prevent violence against women. To be successful, efforts to reduce gender violence must reverse social norms that hold violence to be natural and acceptable. Norm-changing programs should be supported by legal reform, enhanced law enforcement

Rights-based Approaches to HIV

A human rights-based approach to HIV ensures that matters often considered discretionary are recognized as entitlements of all individuals. This approach ensures that governments, the United Nations system, donors, and the private sector are obligated and empowered to help realize the rights necessary to respond to HIV. It brings human rights standards and principles into the heart of all HIV programming processes, and it empowers people to know and claim their rights. It helps stakeholders address power imbalances that exist at household, community, and national levels. In particular, a human rights-based approach to HIV ensures:

- A focus on those who are vulnerable and marginalized in the HIV epidemic (e.g., women, young people, people living with HIV, orphans, men who have sex with men, drug users, sex workers, mobile populations, ethnic and indigenous groups, and refugees);
- Equality and non-discrimination in expenditures on HIV programs and applications;
- Programs to empower those vulnerable to, or living with, HIV, including law reform, legal aid, human rights education, social mobilization, social change communication, and support for civil society;
- Programs designed to achieve human rights standards relevant to HIV (e.g., protection from sexual violence, gender equality, education, information, health, employment, and access to scientific progress);
- Informed, active, free, and meaningful participation by those affected by HIV in HIV-related program design, implementation, monitoring, and evaluation; and
- Accountability mechanisms for governments, intergovernmental organizations, donors, and the private sector. [14]

Source: 2008 Report on the Global Aids Epidemic: Addressing Societal Causes of HIV Risk And Vulnerability. [14]

to hold perpetrators accountable, and activities to address the attitudes and conditions that contribute to gender-based violence.[14]

- *Income-generating strategies.* In many regions, gender inequality may result in women's economic dependence on men, which may in turn heighten their vulnerability to HIV.[14] In places where laws or social customs deprive women of an independent means to generate income and permit husbands to abandon their wives if they are disobedient, women often have little, if any, means to insist on abstinence or condom use by their husbands. According to a recent study in Botswana and Swaziland, women who lack sufficient food are 70% less likely to perceive personal control in sexual relationships, 50% more likely to engage in intergenerational sex, 80% more likely to engage in survival sex, and 70% more likely to have unprotected sex.[23]
- *Advocacy and support.* Globally, many organizations and networks are actively working to build solidarity among women living with HIV, and to undertake joint advocacy to address the epidemic's disproportionate impact on women and girls. National governments and international donors should increase their capacity-building support for women's organizations that are working to advance women's rights and reduce women's vulnerability.[14]

Sex Workers

While it is not possible to accurately count the number of people selling sex, it is estimated that sex workers might number in the tens of millions worldwide—and their clients in the hundreds of millions. While sex workers can be of all ages, most are young, and the great majority are female; their clients (for both male and female sex workers) are mostly male. They work in both urban and rural areas, and in virtually every region. They generally work in areas with large variances in income, creating both a demand by those who seek sexual services and a supply of those impoverished enough to need the money it brings.[24] Sex workers may be self-employed or contracted though brothels, bars, night clubs, or massage parlors.[24] The number of prostituted children is unknown. Although countries may criminalize sex work and subject the act of buying or selling sex for money to criminal sanctions, it is important to note that sex workers are entitled to the same human rights as everyone else, particularly rights to education, information, the highest attainable standard of health, and freedom from discrimination and violence, including sexual violence.[25-26]

Sex Work and Drug Use. In many parts of the world, sex work and injection drug use are intricately linked: drug users resort to sex work to fund their habit, while sex workers turn

to injecting drugs to escape the pressures of their work.[25] Sex workers who also inject drugs are at further risk because the combination of their work and drug use puts them beyond the protection of the law and opens them to exploitation and abuse, including sexual violence and harm. High rates of HIV and sexually transmitted infections have been found among sex workers in countries with large populations of injection drug users. In China, Indonesia, Kazakhstan, Ukraine, Uzbekistan, and Viet Nam, the large overlap between injection drug use and sex work is linked to growing HIV epidemics.[25]

Dr. Stephanie Strathdee of the University of California, San Diego School of Medicine, who addressed the 2010 consultation meeting, noted that female sex workers (FSM) play a unique role in many HIV and STI epidemics because they may both acquire and transmit HIV from and to their clients and non-commercial sex partners, serving as "epidemiological bridges" from high-risk groups to the general population.[27-28] The multiple vulnerabilities faced by this population, including poverty, substance abuse, violence, sexual assault, stigma, and mental illness, directly affect a woman's risk of HIV infection. Drug dependence may compromise the ability of sex workers to negotiate condom use, with both injection and noninjection drug use being associated with HIV risk behaviors. A study of South African sex workers highlighted the intersection of violence against women, substance abuse, and HIV risk and called for targeted, comprehensive interventions for these women.[29] Dr. Strathdee cited studies reporting that HIV prevalence among FSWs who inject drugs ranged from 1.4% in Lithuania to 12.3% in Mexico, 35.4% in the Netherlands, 16.6%-65.0% in Russia, and 10.0% to 22.4% in the U.S.[30] In particular, stimulants such as cocaine and methamphetamine may be used to conserve energy or stay awake.[31] Analyses from 70 countries suggest that the number of HIV-infected FSWs is the strongest predictor of country-wide HIV prevalence in the general population.[32] Given that the global sex industry is increasing,[33] and WHO estimates that less than 15% of FSWs have adequate access to HIV prevention resources,[34] there is a pressing need to identify interventions to reduce HIV incidence among FSWs and their contacts. Interventions that address sexual risk in the context of drug use are lacking.

Male Sex Workers. While not as numerous as female sex workers, male and transgender sex workers also sell sex, predominantly to men.[25] Among these populations, HIV prevalence is frequently high. A recent study in Spain found HIV infection rates of over 12% in male sex workers who visited HIV testing clinics in 19 Spanish cities.[35] In Indonesia, a study found HIV prevalence of 22% among transgender sex workers and 3.6% among male sex workers. Approximately 60% of the transgender sex workers and 65% of the male sex workers reported recent unprotected anal intercourse with clients. Almost 55% of the male sex workers reported having had sex with female partners in the preceding year.[36]

Young and Vulnerable. Most women and men enter sex work in their teens or early 20s. It is estimated that 80% of sex workers in Eastern European and central Asian regions are under 25 years of age, and that sex workers who inject drugs may be even younger than those who do not.[25] Many sex workers lack information about HIV and about services that might help protect them.

Effective Interventions. According to the 2006 UNAIDS Report on the Global AIDS Epidemic, there is substantial evidence that HIV prevention programs for sex workers are effective and that sex workers can be strong participants in HIV prevention programs. The Thai "100% condom use" policy has been replicated with success in countries from Southeast Asia to the Caribbean, while the lessons learned from organized sex workers in India have been replicated in sex-worker projects around the world. Many projects seek to provide sex workers with alternative ways of earning income.[25] Effective strategies include:

- Promotion of safer sexual behavior among sex workers, their partners, and clients (e.g., promotion of condom use and negotiation skills) and of sex-worker solidarity and local organization (in particular, so that clients cannot search for sex workers who are willing to have sex without a condom);
- Provision of sexually transmitted infection prevention and care services, and access to commodities such as male and female condoms and lubricants;
- Peer education and outreach work, including health, social, and legal services;
- Care for sex workers living with HIV; and
- Policy and law reform, along with efforts to ensure that those in authority, such as police and public health staff, respect and protect sex workers' human rights.

These strategies should be accompanied by programs to prevent entry into sex work, assistance to help women escape it, and anti-trafficking measures. Programming works best when it includes the active involvement of sex workers themselves in all phases, from development to evaluation, and

when it aims to decrease their vulnerability by addressing the conditions and context (e.g., economic and gender issues) surrounding sex work.

Men Who Have Sex with Men

The term "men who have sex with men" (MSM) describes a social and behavioral phenomenon, rather than a specific group of people. It includes not only self-identified gay and bisexual men, but also men who engage in male–male sex and self-identify as heterosexual or who do not self-identify at all, as well as transgendered males.[25] Men who have sex with men are found in all countries, yet are largely invisible in many places. According to the 2006 UNAIDS Report on the Global Aids Epidemic, current indicators suggest that globally, fewer than 1 in 20 men who have sex with men have access to the HIV prevention and care services they need.[25] Many factors contribute to this situation, including denial by society and communities, stigma and discrimination, and human rights abuse. Complex gender issues, social and legal marginalization, and lack of access to HIV information affect how many of these men perceive their HIV-related risks. Traditional gender norms of masculinity and femininity contribute to homophobia and the related stigma and discrimination against men who have sex with men and transgendered people. Homophobia has been identified as one of the primary obstacles to effective HIV responses in the move toward universal access to treatment.[25]

Increased Risk-taking. HIV/AIDS has been strongly associated with men who have sex with men since the beginning of the epidemic. In 1981–1982, the first articles appeared in the New England Journal of Medicine and Morbidity and Mortality Weekly Report describing cases of unusual opportunistic infections in homosexual men.[37] HIV incidence among many MSM populations decreased in the late 1980s and early 1990s, predominantly due to the gay community's response to high morbidity and mortality. However, in the post-HAART (highly active retroviral therapy) era, HIV incidence among MSM and MSM who inject drugs has returned to 1985 levels. HIV/AIDS surveillance in the U.S. shows the MSM population to be the only behavioral risk group with increasing incidence,[38] and AIDS is now the number one cause of death in MSM populations.[39]

Sexual risk-taking among men who have sex with men is increasing in many countries, some of it closely linked with alcohol or drug use. For example, the U.S. has witnessed a rapid growth in recent years in the use of the stimulant crystal methamphetamine.[25] Research indicates that in Los Angeles, MSM who use this drug have an HIV infection rate more than three times higher than non-methamphetamine-using men who have sex with men.[40] HIV incidence rates are double or triple for MSM who use amphetamines compared with non-drug-using MSM.[41] Methamphetamine use among MSM, including gay, bisexual, male-to-female transsexuals, and nonidentifying MSM is highly prevalent in the U.S., Australia, and Western Europe.[25]

HIV-positive men who have sex with men surveyed recently in Los Angeles and Seattle in the U.S. were found to be unlikely to disclose their HIV serostatus to sexual partners because they consider it "nobody's business" or because they are in denial, have a low viral load, or fear rejection.[42] Many men who have sex with men also have sex with women and are referred to as MSMW. A large study conducted in Andhra Pradesh, India, found that 42% of men in the sample who had sex with men were married, that 50% had had sexual relations with a woman within the past 3 months, and that just under half had not used a condom.[43] A study of homosexual and bisexual men in Thailand reported that consistent condom use was higher with male partners among MSMW than MSM-only and lower with female partners.[44] African-American MSMW engage in risk behavior with both male and female partners, but those who know they are HIV positive are less likely to have unprotected sex with main partners.[45]

Prevalence of the Epidemic. In some regions of the world, epidemiological information about male-to-male HIV transmission is relatively scarce. This is partly because of the fact that many of the men involved are married to women and are regarded as part of the general population, rather than a distinct subpopulation.[25] In many parts of the world, men who have sex with men have no separate social identity (unlike self-identified "gay" men) and sex between men is not commonly talked about or acknowledged, even by the men themselves.

Dr. Strathdee noted at the consultation meeting that the evolving HIV epidemic among MSM in sub-Saharan Africa has gained increasing attention in recent years. The prevalence of male same-sex behavior in the general population up until 2007 was reported as 0.03-0.9% in Kenya, 0.06-3.6% in South Africa, and 2.3% in Tanzania.[46] HIV prevalence among African MSM ranges from 7.8% in Sudan to 34.3% in Cape Town.[46] HIV incidence was 20.4 per 100 person-years among MSM in Mombasa, Kenya, most of whom were male sex workers.[46]

Effective Interventions. A range of responses aimed at reducing the risk behaviors and vulnerability to HIV of men who have sex with men has proved successful in a variety of settings. These include:

- General and targeted promotion of high-quality condoms and water-based lubricants, and ensuring their continuing availability;
- Safer-sex campaigns and skills training, focusing mainly on reducing the number of partners, increasing condom use, and alternatives to penetrative sex;
- Peer education among men who have sex with men, along with outreach programs by volunteers or professional social or health workers;
- Provision of education and outreach to female partners of men who have sex with men; and
- Programs tailored to particular subpopulations, such as the police, military personnel, prisoners, and male sex workers.

In addition to these prevention measures, a number of activities must be encouraged among managers of health systems and governments.[25] It is important to support organizations of self-identified gay men, enabling them to promote HIV prevention and care programs. Alliances should be developed among epidemiologists, social scientists, politicians, human rights groups, lawyers, clinicians, journalists, organized groups of men who have sex with men, and other civil society organizations. Laws that criminalize same-sex acts between consenting adults in private need to be reviewed, and anti-discrimination or protective laws enacted to reduce human rights violations based on sexual orientation.

Recommendations on human rights and at-risk, vulnerable populations made by breakout groups at the 2010 consultation meeting can be found in Appendix A. The recommendations on at-risk groups encompass the areas of human rights, HIV prevention and implementation, optimizing prevention modalities, and ART therapy as prevention.

Conclusion

Dr. Strathdee noted at the international consultation meeting that because there is considerable overlap among "at-risk" population subgroups, HIV interventions must go beyond approaches that target only one group. Stigma, social and economic disadvantages, and other social processes underlie HIV risks among these populations, representing common drivers of multiple, related epidemics (i.e., "syndemics"). There is a need to better understand and measure the micro and macro factors operating in these risk environments. While we need HIV interventions that are tailored to specific subgroups, prevention programs targeted to syndemic drivers could significantly affect multiple, related epidemics and may be particularly appropriate in low- and middle-income countries. Intervention approaches should consider combinations of behavioral, medical, and structural interventions (e.g., the removal of barriers or laws impeding access to HIV prevention and care).

The HIV epidemic has repeatedly demonstrated that effective responses are those that empower individuals and groups through the realization of their human rights: education, expression, privacy, health, and gender equality, and freedom from discrimination and violence. However, changing harmful norms to reduce vulnerability to HIV and eliminating stigma and discrimination require bold leadership on the part of many stakeholders. Issues that often are considered private or secretive must be brought out into the open and discussed, and laws, government policies, and program priorities may need to change.[14] In particular, key populations at risk—particularly men who have sex with men, sex workers, those in the criminal justice system, and injection drug users—need to have a more meaningful role in collaborative decision-making, planning, and continued monitoring of progress toward the goal of universal access to humane treatment.[14]

References

[1] Office of U.N. Commissioner for Human Rights. http://www2.ohchr.org/english/law/Offfice

[2] Cohen, J. & Wolfe, D. Harm reduction and human rights: Finding common cause. *AIDS* 22 (Suppl 2), S93–94, 2008.

[3] Elliott, R., Csete, J., Wood, E., & Kerr, T. Harm reduction, HIV/AIDS, and the human rights challenge to global drug control policy. *Health and Human Rights* 8, 104-138, 2005.

[4] International Harm Reduction Association and Human Rights Watch. *Recalibrating the Regime: The Need for a Human Rights-Based Approach to International Drug Policy*. London/New York: International Harm Reduction Association and Human Rights Watch, 2008.

[5] Csete, J. & Cohen, J. (eds.). *Lethal Violations: Human Rights Abuses Faced by Injection Drug Users in the Era of HIV/AIDS*, 105–138. New York: International Debate Education Assocation, 2004.

[6] Wolfe, D. & Malinowska Sempruch, K. (eds.). *Seeing Double: Mapping Contradictions in HIV Prevention and Illicit Drug Policy Worldwide*, 330–361. Baltimore: Johns Hopkins University Press, 2007.

[7] Altice, F.L., Mostashari, F., & Friedland, G.H. Trust and the acceptance of and adherence to antiretroviral therapy. *Journal of Acquired Immune Deficiency Syndrome* 28, 47–58, 2001.

[8] Newman, C. Establishing and maintaining a therapeutic alliance with substance abuse patients: A cognitve therapy approach. In *Beyond the Therapeutic Alliance: Keeping the Drug-Dependent Individual in Treatment*. Rockville, MD: National Institute on Drug Abuse, 1994.

[9] Alston, P. & Robinson, M. *Human Rights and Development: Towards Mutual Reinforcement.* New York University Center for Human Rights, 2005.

[10] Neier, A. *Social and Economic Rights: A Critique.* In The Human Rights Brief. Washington, D.C., 2006.

[11] Stemple, L. Health and human rights in today's fight against HIV/AIDS. *AIDS* 22 (Suppl 2), S113–121, 2008.

[12] Gruskin, S. & Ferguson, L. Using indicators to determine the contribution of human rights to public health efforts. *Bulletin of the World Health Organization* 87, 714–719, 2009.

[13] Open Society Institute, 2004. http://www.soros.org/initiatives/health/focus/ihrd/articles_publications/publications/hrnprison_20041022

[14] 2008 Report on The Global Aids Epidemic: Addressing Societal Causes of HIV Risk and Vulnerability. 2008. http://www.unaids.org/en/KnowledgeCentre/HIVData/GlobalReport/2008/2008_Global_report.asp

[15] International Center for Research on Women. HIV/AIDS Stigma: Finding Solutions to Strengthen HIV/AIDS Programs. http://www.icrw.org/docs/2006_stigmasynthesis.pdf

[16] The Global Database on HIV-Related Travel Restrictions. http://www.hivrestrictions.org/

[17] Mahajan, A.P., Sayles, J.N., Patel, V.A., Remien, R.H., Sawires, S.R., Ortiz, D.J., Szekeres, G. & Coates, T.J. Stigma in the HIV/AIDS epidemic: A review of the literature and recommendations for the way forward. *AIDS* 22 (Suppl 2), S67–79, 2008.

[18] Gable, L., Gostin, L., & Hodge, J.G., Jr. A global assessment of the role of law in the HIV/AIDS pandemic. *Public Health* 123, 260–264, 2009.

[19] Merson, M.H., O'Malley, J., Serwadda, D., & Apisuk, C. The history and challenge of HIV prevention. *Lancet* 372, 475–488, 2008.

[20] The Global Coalition on Women and AIDS. http://womenandaids.net/Resource-Centre/Publications.aspx?page=11, LACWHC Gender, Power & HIV Prevention, 2007.

[21] Greig, A., Peacock, D., Jewkes, R., & Msimang, S. Gender and AIDS: Time to act. *AIDS* 22 (Suppl 2), S35–43, 2008.

[22] Garcia-Moreno, C., Jansen, H.A., Ellsberg, M., Heise, L., & Watts, C.H. Prevalence of intimate partner violence: Findings from the WHO multi-country study on women's health and domestic violence. *Lancet* 368, 1260–1269, 2006.

[23] Weiser, S.D., et al. Food insufficiency is associated with high-risk sexual behavior among women in Botswana and Swaziland. *PLoS Medicine* 4, 1589–1597, 2007; discussion 1598.

[24] UNAIDS. Sex Work and HIV/AIDS: UNAIDS Technical Update. Best Practice Collection, 2002. jc705-sexwork-tu_en_small.png

[25] UNAIDS. Report on the Global AIDS Epidemic, 2006. http://www.unaids.org/en/KnowledgeCentre/HIVData/GlobalReport/2006/default.asp

[26] UNAIDS. Guidance Note on HIV and Sex Work. jc1696_guidance_note_hiv_and_sexwork_en_small.png, 2009.

[27] Barrington, C., Latkin, C., Sweat, M.D., Moreno, L. Ellen, J., & Kerrigan, D. Talking the talk, walking the walk: Social network norms, communication patterns, and condom use among the male partners of female sex workers in La Romana, Dominican Republic. *Social Science Medicine* 68, 2037–2044, 2009.

[28] Lowndes, C.M., Alary, M., Gnintoungbe, C.A., Bedard, E., Mukenge, L., Geraldo, N., Jossou, P., Lafia, E., Bernier, F., Baganzi, E., Joly, J., Frost, E., & Anangonou, S.. Management of sexually transmitted diseases and HIV prevention in men at high risk: Targeting clients and non-paying sexual partners of female sex workers in Benin. *AIDS* 14, 2523–2534, 2009.

[29] Wechsberg, W.M., Luseno, W.K., & Lam, W.K. Violence against substance-abusing South African sex workers: Intersection with culture and HIV risk. *AIDS Care* 17 (Suppl 1), S55–64, 2005.

[30] Strathdee, S.A. & Stockman, J.K. The Epidemiology of HIV among "Most at Risk" Drug Using Populations: A Global Perspective. submitted.

[31] Strathdee, S.A.,Philbin, M.M., Semple, S.J., Pu, M., Orozovich, P, Martinez, G., Lozada, R., Fraga, M., de al Torre, A., Staines, H., Magis-Rodriguez, C., & Patterson, T.L. Correlates of injection drug use among female sex workers in two Mexico-U.S. border cities. *Drug and Alcohol Dependence* 92, 132–140, 2008.

[32] Talbott, J.R. Size matters: The number of prostitutes and the global HIV/AIDS pandemic. *PLoS One* 2, e543, 2007.

[33] Ward, H. & Aral, S.O. Globalisation, the sex industry, and health. *Sexually Transmitted Infections* 82, 345–347, 2006.

[34] World Health Organization. Toolkit for Targeted HIV Prevention and Care in Sex Work Settings. Geneva, Switzerland: World Health Organization, Department of HIV/AIDS, 2005. http://www.who.int/hiv/topics/vct/sw_toolkit/en/

[35] Belza, M.J. Risk of HIV infection among male sex workers in Spain. *Sexually Transmitted Infections* 81, 85–88, 2005.

[36] Pisani, E., Girault, P, Gultom, M., Sukartini, N., Kumalawati, J., Jazan, S. & Donegan, E. HIV, syphilis infection, and sexual practices among transgenders, male sex workers, and other men who have sex with men in Jakarta, Indonesia. *Sexually Transmitted Infections* 80, 536–540, 2004.

[37] Persistent, generalized lymphadenopathy among homosexual males. *MMWR Morbidity and Mortality Weekly Report* 31(19), 249–251, 1982.

[38] Shoptaw, S. & Reback, C.J. Methamphetamine use and infectious disease-related behaviors in men who have sex with men: Implications for interventions. *Addiction* 102 (Suppl 1), 130–135, 2007.

[39] Chin, J. *The AIDS Pandemic: The Collision of Epidemiology With Political Correctness.* Oxford: Radcliffe Publishing, 2007.

[40] Peck, J.A., Shoptaw, S., Rotheram-Fuller, E., Reback, C.J., & Bierman, B. HIV-associated medical, behavioral, and psychiatric characteristics of treatment-seeking, methamphetamine-dependent men who have sex with men. *Journal of Addictive Diseases* 24, 115–132, 2005.

[41] Shoptaw, S. & Reback, C.J. Associations between methamphetamine use and HIV among men who have sex with men: A model for guiding public policy. *Journal of Urban Health* 83, 1151–1157, 2006.

[42] Gorbach, P.M., Galea, J.T., Amani, B., Shin, A., Celum, C., Kerndt, P., Golden, M.R. Don't ask, don't tell: Patterns of HIV disclosure among HIV positive men who have sex with men with recent STI practising high risk behaviour in Los Angeles and Seattle. *Sexually Transmitted Infections* 80, 512–517, 2004.

[43] Dandona, L., Dandona, R., Gutierrez, J.P., Kumar, G.A., McPherson, S., Bertozzi, S.M., & ASCI FPP Study Team. Sex behaviour of men who have sex with men and risk of HIV in Andhra Pradesh, India. *AIDS* 19, 611–619, 2005.

[44] Li, A., Varangrat, A., Wimonsate, W., Chemnasiri, T, Sinthuwattanawibool, C., Phanuphak, P., Jommaroeng, R., Vermund, S., & van Griensven, R. Sexual behavior and risk factors for HIV infection among homosexual and bisexual men in Thailand. *AIDS and Behavior* 13, 318–327, 2009.

[45] Lauby, J.L., Millett, G.A., LaPollo, A.B., Bond, L., Murrill, C.S., & Marks, G. Sexual risk behaviors of HIV-positive, HIV-negative, and serostatus-unknown Black men who have sex with men and women. *Archives of Sexual Behavior* 37, 708–719, 2008.

[46] Smith, A.D., Tapsoba, P., Peshu, N., Sanders, E.J., & Jaffe, H.W. Men who have sex with men and HIV/AIDS in sub-Saharan Africa. *Lancet* 374, 416–422, 2009.

Appendix A: Breakout Group Recommendations

Breakout Group 1: Optimizing HIV Prevention Modalities

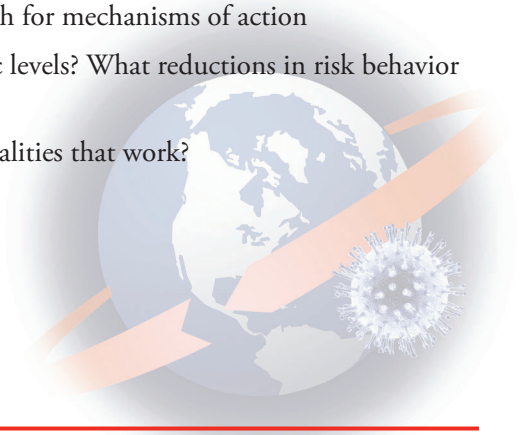
Facilitators: **Wendee Wechsberg, Ph.D.; Don Des Jarlais, Ph.D.**

Recommendations

- Interventions for scaling up in regions/countries with high or increasing prevalence/incidence.
- Sensitivity to culture of the drug-using population/group.

Priority Areas for Research

- Mechanisms of natural recovery
- Structural interventions, what does and does not work
  - Venue-based interventions
  - Role of alcohol ubiquity, use, and dependence as a risk behavior for sexual behavior
- Trafficking (e.g., increased availability of heroin, lower price, higher purity)
- Commercial sex workers
- HIV and comorbidity (e.g., substance abuse and other mental disorders; STDs other than HIV/AIDS)
- Trauma
- Using general health care settings as entry to HIV/AIDS testing and substance abuse prevention and treatment
- Targeting interventions to high-risk populations—which are highest risk, how to target them?
- Groups associated with increased risk of overdose (e.g., released from incarceration, out of detoxification)
- Portability/availability of EBIs for use by communities, health care providers
  - Use of technology, especially mobile technology, to increase access to EBIs
- Integrated care models
  - Using technology for multiple intervention effects
- Growth of stimulant use/abuse, including injection stimulant use
- Modes of drug use and risky behavior (e.g., trading sex for drugs, power dynamics of drug behavior and acquisition, patterns of change in drug-seeking and drugs of preference in a population)
- Differences in risk behaviors, surveillance, prevention, and treatment modalities in different countries/cultures
- Research to maximize positive effect sizes found in initial association studies; search for mechanisms of action
- How low does risk behavior need to be addressed to stop transmission at epidemic levels? What reductions in risk behavior matter?
- Non-injecting drug users and sexual transmission: What are the intervention modalities that work?
  - How to sustain/reinforce behavior change over extended periods?



- Environmental/cultural/socioeconomic factors in risky behavior (e.g., CSWs in different cultures)

Other Issues

- Succession: Where will the next generation of researchers/implementers come from? How to foster/train the next generation?
- Costing and cost-effectiveness assessment of interventions as a basis for policy recommendations to governments and other funders/adopters
- High resource requirements for implementation in diverse cultures
- Sustainability of an intervention beyond the study period or initial implementation

Breakout Group 2: Drug Abuse Treatment as HIV Prevention

Facilitators: **David Metzger, Ph.D.; Jeffrey Samet, M.D.**

General Topic Areas

- Scale-up of health services/research
- Effective components of substance abuse therapy
- Substance abuse service integration
- Medical integration
- Underserved populations

Overarching Issue

- Need to keep both global and domestic perspectives on how these issues are addressed

Recommendations: Scale Up Health Services

- Match scale-up strategies to epidemiologic need.
- Assess the impact of current interventions.

Recommendations: Effective Treatment

- Develop accountability system for quality of services.
- Promote effective treatment that combines counseling, pharmacotherapy, and wraparound services (as a subset of this, make mobile units available).
- Integrate HIV prevention measures into all substance abuse treatment, including information on access to condoms, needle exchange, etc.
- Treat comorbid infections and conditions.

Recommendations: Service Integration

- Every client in substance abuse treatment has access to primary care.
- Train general health care providers in substance abuse recognition and SBIRT.

Recommendations: Underserved Populations

- All prisoners on MAT continue throughout incarceration.

Priority Areas for Research: Scale Up Health Services

- Test models for scale-up.

- Cost-effectiveness analysis of scale-up in various locales.
- Barriers and facilitators of effective adoption and intervention.

Priority Areas for Research: Effective Treatment

- Continue the search for pharmacotherapies, vaccines, etc., other than opioids.
- Develop client–treatment matching according to individual client characteristics.
- What are the characteristics of the workforce that are necessary to achieve maximal outcomes?

Priority Areas for Research: Underserved Populations

- Study and optimize treatment interventions specific to women, cultural and ethnic minorities, LGBTI individuals, incarcerated individuals, and other underserved peoples.

Breakout Group 3: HIV Prevention Implementation: Integration and Rolling Out

Facilitators: **Judy Auerbach, Ph.D.; Richard Wolitski, Ph.D.**

Recommendations

- Implement and optimize the eight WHO elements of comprehensive prevention, treatment, and care for drug users, adhering to best-practice guidelines and integrating multiple interventions:
  1. Expand syringe access
     - NSP
     - Pharmacy access
     - Remove rigid restrictions, such as possession of paraphernalia and prescriptions for syringes
  2. Opioid substitution therapy (OST)
  3. HIV Testing
  4. Anti-retroviral therapy (ARV)—Decrease barriers to ensure inclusion for treatment of drug users with appropriate medications
  5. Targeted outreach, counseling, and education
  6. Co-infections—diagnosis and treatment
  7. STI, TB, and hepatitis
  8. Condoms—male and female
- Ensure access and coverage through various modes of distribution; rapidly scale up programs; eliminate policy and practice restrictions.
- Reform policies that compromise access to and coverage of prevention programs—e.g., drug possession and paraphernalia laws.
- Alternatives to detention/incarceration as drug treatment.
- Continuous access to HIV treatment in and out of jails/prisons.
- Funding silos, categorical program funding.
- Free access to male and female condoms and syringes in all settings.
- Screen all people in HIV care for drug use and provide appropriate drug services/treatment.

Priority Areas for Research

- Assess/evaluate effectiveness of decriminalization of personal possession and use of currently criminalized drugs.
- Evaluate effectiveness of comprehensive programs (e.g., supervised injection facilities) for (a) linkage to services, (b) ART uptake, (c) HIV prevention, and (d) health outcomes.
- Evaluate outcomes of drug control policies for health and well-being of drug users.
- Develop improved treatment for cocaine and stimulants, both behavioral and pharmacological.
- Develop improved regimens vis-à-vis interactions among addiction treatment, ART, TB treatment, contraception, etc.
- Mechanisms to approach social and policy change to optimize health and well-being of drug users.
- Implementation of new prevention methods (e.g., PreP in drug users).
- Development and implementation in the field of combined prevention strategies ("how to").
- Maximize inclusion of drug users and other populations vulnerable to parenteral exposure in wider HIV research agenda (i.e., transmission, pathogenesis, etc.).
- Better address combinations of drug use and sexual risk in HIV transmission/acquisition.
- Evaluate implementation of primary prevention among young people that have demonstrated efficacy in reducing subsequent substance use and sexual risk behavior.
- Design and implement interventions for people, including those living in transitional societies, who have a history of trauma, violence, abuse, and prejudice to reduce HIV, risk behavior, and drug use and improve health outcomes.
- Translational and dissemination research on all of the above.

Breakout Group 4: ART Therapy as HIV Prevention: Seek, Test, and Treat

Facilitators: **David Wohl, M.D.; Curt Beckwith, M.D.**

Evidence for ART as Prevention

- ART works to reduce the virus in HIV-positive people by high orders of magnitude.
- Viral load and risk of transmission are inversely related; this includes transmission from mother to child, heterosexual transmission, etc. (However, it's possible that transmission can occur during treatment.)
- Heterosexual data are strongest; there is less information about MSM and IDUs.
- Substance users are often tested, diagnosed, and treated late in the progression of HIV.
- HIV treatment in substance users has the potential to be as effective as HIV treatment in other populations.
- There is an association between active substance use and suboptimal adherence.
- Substance use treatment/management is associated with improved ART outcomes.
- HIV and substance use stigma and discrimination are barriers to seek and treat.
- Addressing competing needs and comorbidities leads to improved outcomes.

Recommendations

- We need to critically examine the structural forces that promote the HIV epidemic among drug users and identify opportunities to limit their effects.
- We must do a better job of:
  - seeking persons who are at risk of HIV infection;
  - bringing testing to the people who have less access to testing services;
  - bringing treatment to the people for whom it is medically indicated; and

  - maintaining persons in treatment.
- It is imperative that testing and treatment efforts be monitored for efficacy, safety, and relative cost-effectiveness.
- We need better and optimized national programs to monitor incidence and prevalence of HIV and outcomes among substance-using HIV-positive persons.
- These should be implemented within a comprehensive prevention framework and with full regard to human rights.

Priority Areas for Research

- Research to improve the operations, implementation, and translation of seek, test, and treat.
- Assessment of different strategies for effectively seeking substance users with undiagnosed HIV.
- New strategies for testing approaches for substance users are needed.
- Detecting acute HIV among substance users.
- New strategies for linking substance users to treatment services and retaining them.
- HIV incidence monitoring (e.g., monitoring of collateral benefits) is needed.
- Monitoring of collateral benefits.

Breakout Group 5: Human Rights and Vulnerable Populations

Facilitators: **Celia Fisher, Ph.D.; Scott Burris, J.D.**

Access to evidence-based treatment and prevention is a fundamental human right. Individuals are embedded in physical, social, economic, and policy environments that shape the risks of drug use, access to and effectiveness of testing, drug use, and HIV treatment programs.

NIDA can make a difference by encouraging system-model research that brings HIV linkages to human rights to the foreground to complement and infuse clinical models. The presence or absence of human rights is a social driver of resilience and vulnerability of HIV.

Human rights or their absence are operationalized for the purposes of drug abuse/HIV research, including laws and law enforcement as practices; social exclusion, discrimination in housing, employment, and health care; freedom from violence; sex and gender inequality; and other factors.

Research Priorities

- Research on the negative impacts of laws, policies, and practices that impede effective substance abuse and HIV services:
  - Research on police, legal, and health care practices that impact drug users' health services utilization;
  - Research on housing, social assistance, education, employment, etc., practices that impact drug users' health services and utilization;
  - Move from focus on individual risk, adherence, etc., to measures of systemic discrimination;
  - Research on social factors and processes that produce and perpetuate policies that foster human rights violations.
- Research on the social and structural policies and interventions that promote human rights that positively and negatively impact drug abuse and HIV health services outcomes:
  - Research on the means of mobilizing capacity and promoting personal and collective efficacy in marginalized populations subject to human rights protections;
  - Strengthen research on the health impacts of human rights protections, legal aid, police trainings and reform, sexual victimization;
  - Research on mechanisms of accountability in systems and services;
  - Evaluate the effects of decriminalization, pretrial justice reform, and other criminal justice sector reform.

- Break down institutional and disciplinary barriers that separate health from research and data sources from criminal justice, law, and policy.
- Research on the risks and remedies of potential human rights violations associated with seek, test, and treat; and SBIRT.
- Research designs that include human rights protections around screening, HIV testing, prevention, and treatment inside and outside of health care facilities.
- NIDA should support research that looks at post-investigative data on drug abuse and HIV research-based prevention, testing, and interventions.
- Research should be conducted in a way that is consistent with ethical and human rights standards that take into account the long-term needs of participants.

Breakout Group 6: HIV/AIDS Treatment

Facilitators: **Greg Lucas, M.D., Ph.D.; Adeeba Kamarulzman, M.D.**

Key Topics

- Prevention in positives
- Treating substance abuse
  - Coordination/integration of substance abuse and HIV care
  - Pharmacotherapies and behavioral therapies
- When to start ART
- What to use
- Drug–drug interactions of meds, drugs of abuse
- Engagement and retention in treatment
- Access and structural barriers to ART

Recommendations

- Devote a portion of the NIDA and IAS websites to information on drug–drug interactions.
- Teach health care professionals to utilize SBIRT with ART patients.

Priority Areas for Research

- Study drug–drug interactions of meds, drugs of abuse.
  - Focus on illicit drug–HIV med interactions and addiction med–HIV med interactions (e.g., buprenorphine, methadone, naltrexone, acamprosate, alcohol, nicotine).
- To what extent is engagement in HIV care a teachable time that allows for the introduction of substance abuse treatment?
- Likewise, to what extent is engagement in substance abuse treatment a teachable time that allows for the introduction of HIV care?
- What instruments should be used for screening patients for substance use, abuse, and severity?
- Determine the pros and cons of medical marijuana as an adjunct to ART.
- Study clinical priority-setting in HIV-positive substance abusers' treatment needs (vis-à-vis co-infections, medical comorbidities, psychiatric comorbidities).
- Study medical provider decision-making and its impact on outcomes and quality of care.
- Examine individual, social, and structural factors preventing substance abuse patients from starting ART.
- Examine active drug use as a barrier for physicians treating HIV-positive substance users.

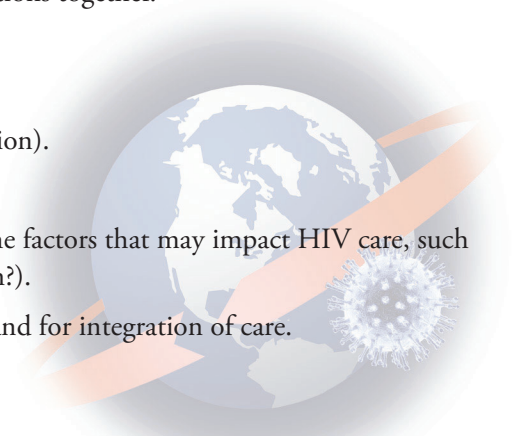
- Examine the relationship, if any, between the pattern of drug use and ART outcomes.
- Compare first-line treatments (e.g., PI versus NNRTI) in substance abusers.
- Study interventions that retain substance abusers: engage in treatment, continue treatment, and have treatment success.

Breakout Group 7: Comorbidity and Adherence

Facilitators: Jim Sorensen, Ph.D.; David Thomas, M.D., M.P.H.

Research Priorities

- NIDA should call for FDA and other regulatory agencies to investigate the effectiveness and safety of treatments for HIV, HCV, TB, and STDs in IDUs and to study interactions for drug clinical development.
- Assess the relative benefits/barriers of multidisciplinary approaches to achieving system-level outcomes on substance abuse-related HIV outcomes.
- Test different models of care based on task shifting in resource-limited settings and evaluate effectiveness, including costs.
- Develop interventions that foster adherence across comorbid conditions, recognizing that not all comorbid conditions are created equally (psychiatric morbidity and hepatitis).
- Understand the IDU and non-IDU transmission of HCV among MSM.
- Investigate the comparative effectiveness of models to cure HCV infection among injection drug users in methadone clinics, prisons, and other special venues (multi-PI work).
- Scale of research proportionate to outcomes and impacts (e.g., conditions with high morbidity and mortality and opportunity for impact should be highest priority).
- Clinical trials should include drug users and comorbid individuals.
- Explain the phenomena of comorbidity and how syndemics are produced.
- Develop strategies for explaining toxicities in treatment, how additional treatment affects patients, and explore linking for each treatment.
- Investigate macroscopic elements of comorbidity treatment, such as funding and staffing, and its effect on treatment.
- Investigate other systems issues, such as insurance, cross-training of staff, and licensing.
- Look at levels of competency to ensure safety of clients and effects on treatment.
- Include drug users in studies of comorbid conditions such as HIV and TB—management should be considered concomitantly, particularly in Phase III and IV studies.
- Move some of subpopulation requirements for drug development to Phase IV, so as not to delay approval of drug.
- Investigate unintended consequences of delayed approval—look at quality of life of individuals, patient-reported outcomes.
- Study interaction toxicities among new drugs and current street drugs.
- Screen and assess for comorbid conditions; there is a need to put all of these conditions together.
- Develop multi-PI approaches or team approaches.
- Develop models of collaboration.
- Pharmacokinetic data needed for comorbid individuals (e.g., high levels of depression).
- How do we overcome barriers to screening for prevention?
- Look at community-based prevention/interventions that take into account all of the factors that may impact HIV care, such as violence, depression, and substance abuse (demonstration projects as mechanism?).
- Look at prison settings as a controlled community to study comorbid individuals and for integration of care.



- Look at adherence in individuals with substance abuse and major psychiatric disorders.
- Look at adherence in all types of drug abuse, looking at burdens of different types of abuse.
- Research to explore integration of systems of care as well as behavioral treatments. Identify common modules (e.g., anxiety, depression).
- Develop a theory-based profile and test the profile for early adherence in a trial. Look at adherence issues up front
- Translational research and implementation.
- Look at Eastern European and other countries and particularly task-shifting models of care (using less expensive systems of care). Develop new models of care for the U.S. that involve communities.

Breakout Group 8: Criminal Justice: HIV Prevention and Treatment

Facilitators: **Redonna Chandler, Ph.D.; Frederick Altice, M.D., MPHIL**

Opportunities for Intervention

- Sites of intervention (jail, prison, probation, parole, drug court, juvenile justice, other):
  - Match to site
  - Match to individual
- Re-link individuals into health care system:
  - How to integrate?
- Primary and secondary prevention
- HIV/STI testing and identification
- Behavioral risk reduction
- Access to and continuation of HAART
- Impact of criminal justice on communities:
  - Social networks
  - Health disparities among people of color
- Transitional interventions (individual, systems):
  - MAT (opioids, alcohol, mental illness)
  - Behavioral
  - Structural
  - Special populations (e.g., women, adolescents)
  - Discharge planning methods

Priority Areas for Research

- Find the most optimal strategy for combined testing for HIV, STD, TB, and hepatitis across criminal justice spectrum:
  - How and when to do HIV testing across criminal justice?
- Optimal strategy for linking HIV+ in any of these areas to care (HIV and comorbidities) within corrections and communities (including transition) on a sustainable basis:
  - Tailored to the individual and treatment setting.
- Create evidence-based interventions within criminal justice that match individuals to interventions for those with or at risk for HIV.
- Overarching issue: Relationship between HIV epidemic within minority populations and their involvement in criminal justice.

Appendix B: Meeting Agenda

NIDA/IAS Consultation Meeting
Prevention and Treatment of HIV/AIDS Among Drug Using Populations: A Global Perspective

Mayflower Hotel
Washington, DC
January 11 – 12, 2010

AGENDA

Day 1 - Monday, January 11, 2010

8:15 – 8:25 a.m. **Welcome**

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

Julio Montaner, M.D.
President
International AIDS Society (IAS)

8:25 – 8:30 a.m. **Introduction of Meeting Co-Chairs**

Nora D. Volkow, M.D.
NIDA

8:30 – 8:45 a.m. **Raison d'être of Meeting and Introduction of Opening Panel**

Meeting Co-Chairs:

Charles O'Brien, M.D., Ph.D.
University of Pennsylvania

Julio Montaner, M.D.
British Columbia Centre for Excellence in HIV/AIDS

8:45 – 11:15 a.m. **Opening Panel**

Moderator: Nora D. Volkow, M.D.
NIDA

Ambassador Eric Goosby, M.D.
President's Emergency Plan for AIDS Relief

Jeffrey Crowley, M.P.H.
Office of National AIDS Policy

A. Thomas McLellan, Ph.D.
Office of National Drug Control Policy

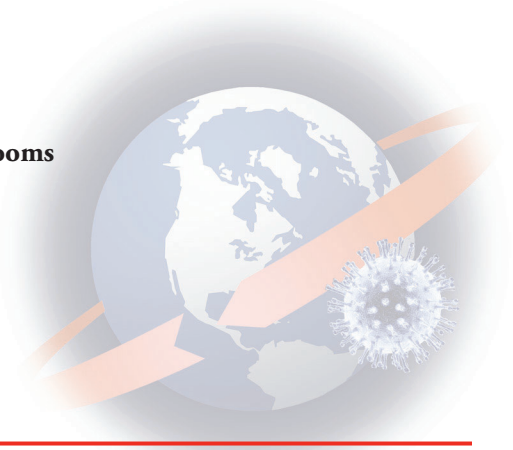
Kevin Fenton, M.D., Ph.D.
Centers for Disease Control and Prevention

	Jack Whitescarver, Ph.D. *Office of AIDS Research* Anthony Fauci, M.D. *National Institute of Allergy and Infectious Diseases* Catherine Hankins, M.D., M.Sc. *The United Nations Joint Programme on HIV/AIDS*
11:15 – 11:30 a.m.	**Break**
11:30 – 12:00 p.m.	**Epidemiological Link between Drug Abuse and HIV: An International Perspective** Chris Beyrer, M.D., M.P.H. *Johns Hopkins Center for Public Health and Human Rights*
12:00 – 12:30 p.m.	**Expanded Highly Active Anti-Retroviral Therapy Coverage Among HIV-Infected Drug Users to Improve Individual and Public Health Outcomes** Julio Montaner, M.D. *British Columbia Centre for Excellence in HIV/AIDS*
12:30 – 12:45 p.m.	**Challenges for Seek, Test, and Treat for Drug Users** Nora D. Volkow, M.D. *NIDA*
12:45 – 1:45 p.m.	**Working Lunch (Instructions for Breakouts)**
1:45 – 2:15 p.m.	**Substance Abuse Treatment as HIV Prevention** Charles O'Brien, M.D., Ph.D. *University of Pennsylvania*
2:15 – 2:45 p.m.	**Towards a Comprehensive Approach to HIV Prevention for People Who Use Drugs** Evan Wood, M.D., Ph.D. *British Columbia Centre for Excellence in HIV/AIDS*
2:45 – 4:15 p.m.	*Breakout Sessions* **I. Drug Abuse Treatment as HIV Prevention** David Metzger, Ph.D. *University of Pennsylvania* Jeffrey Samet, M.D. *Boston University* **II. ART Therapy as HIV Prevention: Seek, Test, and Treat** David Wohl, M.D. *University of North Carolina* Curt Beckwith, M.D. *Brown University* **III. HIV Prevention Implementation: Integration and Rolling-out** Judy Auerbach, Ph.D. *San Francisco AIDS Foundation* Richard Wolitski, Ph.D. *Centers for Disease Control and Prevention*

	IV. Optimizing HIV Prevention Modalities Wendee Wechsberg, Ph.D. *RTI International* Don Des Jarlais, Ph.D. *Beth Israel Medical Center*
4:15 – 4:30 p.m.	**Break**
4:30 – 5:15 p.m.	**Reports From Breakout Groups and Discussion**
5:15 p.m.	**Adjournment**

Day 2 – Tuesday, January 12, 2010

8:15 – 8:30 a.m.	**Recap of Day 1** Co-Chairs
8:30 – 9:00 a.m.	**HIV/AIDS Treatment** Roy M. Gulick, M.D. *Weill Cornell Medical College*
9:00 – 9:30 a.m.	**Issues in Adherence to Antiretroviral Therapy for Drug-Abusing Populations** Robert Gross, M.D. *University of Pennsylvania*
9:30 – 10:00 a.m.	**Co-infections, Comorbidity, Drug Interactions** Gerald Friedland, M.D. *Yale School of Medicine*
10:00 – 10:15 a.m.	**Break**
10:15 – 11:15 a.m.	***Vulnerable Groups*** **Criminal Justice** Josiah Rich, M.D. *Brown University* **Sex Workers, MSM, Mobile Populations and Minorities** Steffanie Strathdee, Ph.D. *University of California, San Diego*
11:15 – 11:45 a.m.	**Implementation Science/Operational Research** Bruce Schackman, Ph.D. *Weill Cornell Medical College*
11:45 – 12:15 p.m.	**Human Rights** Daniel Wolfe, M.P.H. *Open Society Institute*
12:15 – 12:30 p.m.	**Pick Up Lunch and Bring to Breakout Rooms**



12:30 – 2:15 p.m.	***Breakout Sessions***
	I. HIV/AIDS Treatment
	Greg Lucas, M.D., Ph.D. *Johns Hopkins School of Medicine*
	Adeeba Kamarulzman, M.D. *University of Malaysia*
	II. Co-morbidity Adherence
	Jim Sorensen, Ph.D. *University of California, San Francisco*
	David Thomas, M.D., M.P.H. *Johns Hopkins Bloomberg School of Public Health*
	III. Human Rights/Vulnerable Populations
	Celia Fisher, Ph.D. *Fordham University*
	Scott Burris, J.D. *Temple University*
	IV. Criminal Justice: HIV Prevention and Treatment
	Redonna Chandler, Ph.D. *NIDA*
	Frederick Altice, M.D., M.Phil. *Yale University*
2:15 – 2:30 p.m.	**Break**
2:30 – 3:15 p.m.	**Reports From Breakout Groups and Discussion**
3:15 – 3:30 p.m.	**Sum-Up**
	Co-Chairs
3:30 p.m.	**Adjournment**

Appendix C: Participant List 2010 Consultation Meeting

NIDA/IAS Consultation Meeting
Prevention and Treatment of HIV/AIDS Among Drug Using Populations: A Global Perspective

Mayflower Hotel
Washington, DC
January 11 – 12, 2010

Participant List

Jeffrey Allen, M.D.
Chief
Health Programs
Federal Bureau of Prisons
320 First Street NW
Washington, DC 20534
Work Phone: (202) 353-4743
Email: jd1allen@bop.gov

Frederick Altice, M.D., M.Phil.
Professor of Medicine
Internal Medicine-AIDS Program
Yale School of Medicine
135 College Street, Suite 323
New Haven, CT 06510
Work Phone: (203) 737-2883
Email: paula.dellamura@yale.edu

Judith Auerbach, Ph.D.
Vice President
Science & Public Policy
San Francisco AIDS Foundation
995 Market Street, Suite 200
San Francisco, CA 94103
Work Phone: (415) 487-3080
Email: jauerbach@sfaf.org

Ruban Baler, Ph.D.
Health Scientist Administrator
Science Policy Branch
Office of Science Policy and Communications
National Institute on Drug Abuse
National Institutes of Health
6001 Executive Boulevard
Room 5421
Bethesda, MD 20892
Work Phone: (301) 594-6790
Email: balerr@mail.nih.gov

Jacqueline Bataringaya, M.D.
Senior Policy Advisor
International AIDS Society
Avenue Louis-Casaii, 71
Geneva, Switzerland
Work Phone: 41 22 710 08 01
Email: Jacqueline.Bataringaya@iasociety.org

Lula Beatty, Ph.D.
Chief
Special Populations Office
National Institute on Drug Abuse
National Institutes of Health
6001 Executive Boulevard, Room 4216
Bethesda, MD 20892
Work Phone: (301) 443-0441
Email: lbeatty@nida.nih.gov

Curt Beckwith, M.D.
Assistant Professor of Medicine
Infectious Diseases
The Miriam Hospital
Alpert Medical School
Brown University
164 Summit Avenue
Providence, RI 02906
Work Phone: (401) 793-4397
Email: CBeckwith@Lifespan.org

Chris Beyrer, M.D., M.P.H.
Professor
Epidemiology
Johns Hopkins Bloomberg School of Public Health
615 N. Wolfe Street, E 7152
Baltimore, MD 21205
Work Phone: (410) 614-5247
Email: cbeyrer@jhsph.edu

Robert Booth, Ph.D.
Professor
Department of Psychiatry
University of Colorado at Denver
1741 Vine Street
Denver, CO 80206
Work Phone: (303) 315-0960
Email: robert.booth@ucdenver.edu

Lawrence Brown, Jr., M.D.
Executive Senior Vice President
Addiction Research and Treatment Corporation
22 Chapel Street
Brooklyn, NY 11201
Work Phone: (718) 260-2917
Email: Lbrown@artcny.org

Julie Bruneau, M.D., M.Sc.
Associate Professor
Centre Hospitalier de l'Université de Montréal
University of Montréal
264 René-Lévesque Est
Montréal, QC H2X 1P1
Work Phone: (514) 890-8000
Email: julie.bruneau@umontreal.ca

Rachel Burdon, M.D.
Senior Technical Officer
Care and Treatment
Family Health International
30 Nguyen Du, Hai Ba Trung
Hanoi, Vietnam
Work Phone: (090) 341-3993
Email: rachel@fhi.org.vn

David Burns, Ph.D.
Chief
Prevention Research Branch
Division of AIDS
National Institute of Allergy and Infectious Diseases
National Institutes of Health
6700B Rockledge Drive, Room 5121
Bethesda, MD 20892
Work Phone: (301) 435-8896
Email: burnsda@niaid.nih.gov

Scott Burris, J.D.
Professor
Beasley School of Law
Temple University
1719 North Broad Street
Philadelphia, PA 19122
Email: scott.burris@temple.edu

Patrizia Carrieri, Ph.D.
Epidemiologist
INSERM
U912 - ORSPACA
23 rue Stanislas Torrents
13006 Marseilles, France
Work Phone: 33 4 91598900
Email: pmcarrieri@aol.com

Redonna Chandler, Ph.D.
Branch Chief
Services Research Branch
Division of Epidemiology, Services and Prevention Reserach
National Institute on Drug Abuse
National Institutes of Health
6001 Executive Boulevard, Room 5185
Bethesda, MD 20892
Work Phone: (301) 443-6504
Email: brandin.dechabert@nih.gov

Myron (Mike) Cohen, M.D.
Associate Vice Chancellor
Infectious Diseases
University of North Carolina at Chapel Hill
130 Mason Farm Road
Chapel Hill, NC 27517
Work Phone: (919) 966-2536
Email: mscohen@med.unc.edu

Grant Colfax, M.D.
Director
HIV Prevention and Research
San Francisco Department of Public Health
25 Van Ness Avenue, Suite 500
San Francisco, CA 94102
Work Phone: (415) 554-9173
Email: grant.colfax@sfdph.org

Wilson Compton, M.D.
Director
Division of Epidemiology, Services and Prevention Research
National Institute on Drug Abuse National Institutes of Health
6001 Executive Boulevard
Room 5158
Bethesda, MD 20892
Work Phone: (301) 443-6504
Email: wcompton@nida.nih.gov

Timothy Condon, Ph.D.
Deputy Director
National Institute on Drug Abuse
National Institutes of Health
6001 Executive Boulevard, Room 5274
Rockville, MD 20852
Work Phone: (301) 443-6487
Email: lindenl@nida.nih.gov

Jeffrey Crowley, M.P.H.
Director
Office of National AIDS Policy
The White House
Washington, DC 20502
Work Phone: (202) 456-4533
Email: Jeffrey_s._crowley@who.eop.gov

Joanne Csete, Ph.D.
Associate Professor
Department of Population and Family Health
Columbia University Mailman School of Public Health
60 Haven Avenue, B2
New York, NY 10032
Work Phone: (212) 304-5278
Email: jc1188@columbia.edu

Katherine Davenny, M.P.H.
Associate Director
AIDS Research Program
Office of the Director
National Institute on Drug Abuse
National Institutes of Health
6001 Executive Boulevard,Room 4215
Bethesda, MD 20892
Work Phone: (301) 443-2146
Email: kd25h@nih.gov

Carlos del Rio, M.D.
Professor and Chair
Hubert Department of Global Health
Rollins School of Public Health
Emory University
1518 Clifton Road NE, Room 754
Atlanta, GA 30033
Work Phone: (404) 727-7112
Email: cdelrio@emory.edu

Don C. Des Jarlais, Ph.D.
Director of Research
The Baron Edmond de Rothschild Chemical Dependency Institute
Beth Israel Medical Center
160 Water Street, Room 2462
New York, NY 10038
Work Phone: (212) 256-2548
Email: dcdesjarla@aol.com

Sergei Dvoryak, M.D., Ph.D.
Director
Ukrainian Institute on Public Health Policy
91/14 Gorkiy Street, Apartment 5-6
Kyiv, 03150 Ukraine
Work Phone: 38 044 529 6750
Email: dvoryak@uiphp.org.ua

Nabila El-Bassel, Ph.D.
Professor
Columbia University
1255 Amsterdam Avenue, Office 814
New York, NY 10027
Work Phone: (212) 851-2391
Email: ne5@columbia.edu

Lynda Erinoff, Ph.D.
Associate Director
AIDS Research Program
Office of the Director
National Institute on Drug Abuse
National Institutes of Health
6001 Executive Boulevard
Room 5274/MSC 9581
Bethesda, MD 20892
Work Phone: (301) 402-1972
Email: le30q@nih.gov

Anthony Fauci, M.D.
Director
National Institute of Allergy and Infectious Diseases
National Institutes of Health
31 Center Drive
MSC 2520/Room 7A03
Bethesda, MD 20892
Work Phone: (301) 496-2263
Email: afauci@niaid.nih.gov

Kevin Fenton, M.D., Ph.D.
Director
National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention
Centers for Disease Control and Prevention
1600 Clifton Road NE
Mail Stop E07
Atlanta, GA 30333
Work Phone: (404) 639-8000
Email: kif2@cdc.gov

Celia Fisher, Ph.D.
Director
Center for Ethics Education
Fordham University
441 East Fordham Road
Dealy Hall
Bronx, NY 10458
Work Phone: (718) 817-3793
Email: fisher@fordham.edu

Timothy Flanigan, M.D.
Director
Infectious Diseases
The Miriam Hospital
Alpert Medical School
Brown University
164 Summit Avenue
Providence, RI 02906
Work Phone: (401) 793-7152
Email: tflanigan@lifespan.org

Joseph Frascella, Ph.D.
Director
Division of Clinical Neuroscience and Behavioral Research
National Institute on Drug Abuse
National Institutes of Health
6001 Executive Boulevard
Bethesda, MD 20853
Work Phone: (301) 443-4877
Email: jfrascel@nida.nih.gov

Gerald Friedland, M.D.
Professor of Medicine and Epidemiology
Internal Medicine, Infectious Diseases
Yale School of Medicine
Director
AIDS Program at Yale New Haven Hospital
135 College Street, Suite 323
New Haven, CT 06510-2483
Work Phone: (203) 688-6959
Email: gerald.friedland@yale.edu

Vivian Go, Ph.D., M.P.H.
Associate Professor
Department of Epidemiolgy
Johns Hopkins Bloomberg School of Public Health
615 N. Wolfe Street, E6610
Baltimore, MD 19095
Work Phone: (215) 572-5736
Email: vgo@jhsph.edu

Ambassador Eric Goosby, M.D.
U.S. Global AIDS Coordinator
U.S. President's Emergency Plan for AIDS Relief
Department of State
2201 C Street NW
Washington, DC 20520
Work Phone: (202) 647-4000
Email: goosbye@state.gov

Christopher M. Gordon, Ph.D.
Chief
Secondary HIV Prevention and Translational Research Branch
Associate Director for Prevention
National Institute of Mental Health
National Institutes of Health
6001 Executive Boulevard, Room 6212
Bethesda, MD 20892-9619
Phone: (301) 443-1613
Email: cgordon1@mail.nih.gov

William Grace, Ph.D.
Behavioral and Social Sciences
NIH Office of AIDS Research
Office of the Director
National Institutes of Health
5635 Fishers Lane
Bethesda, MD 20892
Work Phone: (301) 402-4149
Email: wg15v@nih.gov

Robert Gross, M.D.
Associate Professor of Medicine and Epidemiology
Infectious Diseases
Center for Clinical Epidemiology and Biostatistics
University of Pennsylvania
School of Medicine
423 Guardian Drive, 804 Blockley Hall
Philadelphia, PA 19104-6021
Work Phone: (215) 898-2437
Email: grossr@mail.med.upenn.edu

Roy Gulick, M.D.
Professor of Medicine
Division of Infectious Diseases
Weill Cornell Medical College
1300 York Avenue, Box 125
New York, NY 10065
Work Phone: (212) 746-6320
Email: rgulick@med.cornell.edu

Steve Gust, Ph.D.
International Program
National Institute on Drug Abuse
National Institutes of Health
6001 Executive Boulevard
Bethesda, MD 20895
Work Phone: (301) 443-6480
Email: sgust@nih.gov

Catherine Hankins, M.D., M.Sc.
Chief Scientific Adviser
The Joint United Nations Programme on HIV/AIDS
20 Avenue Appia
CH-1211 Geneva 27
Switzerland
Work Phone: (079) 202-1845
Email: hankisc@unaids.org

Peter Hartsock, Dr.P.H.
Research Scientist Officer
Epidemiology Research Branch
Division of Epidemiology, Services and Prevention Research
National Institute on Drug Abuse
National Institutes of Health
6001 Executive Boulevard, Room 5185
Bethesda, MD 20892
Work Phone: (301) 402-1964
Email: ph45z@nih.gov

Rhonda Holliday, Ph.D.
Research Associate Professor
Morehouse School of Medicine
1513 East Cleveland Avenue
East Point, GA 30344
Work Phone: (404) 756-5042
Email: rholliday@msm.edu

David Holtgrave, Ph.D.
Professor and Department Chair
Department of Health, Behavior and Society
Johns Hopkins Bloomberg School of Public Health
624 North Broadway
Baltimore, MD 21205
Work Phone: (410) 502-4076
Email: dholtgrave@jhsph.edu

Richard Jenkins, Ph.D.
Health Scientist Administrator
Prevention Research Branch
Division of Epidemiology, Services and Prevention Research
National Institute on Drug Abuse
National Institutes of Health
6001 Executive Boulevard
MSC 9589 Room 5185
Bethesda, MD 20892
Work Phone: (301) 443-1923
Email: jenkinsri@mail.nih.gov

Dionne Jones, Ph.D.
Deputy Branch Chief
Services Research Branch
Division of Epidemiology, Services
and Prevention Research
National Institute on Drug Abuse
National Institutes of Health
6001 Executive Boulevard, Room 5195
Bethesda, MD 20893
Work Phone: (301) 443-6504
Email: djones1@nida.nih.gov

Shoshana Kahana, Ph.D.
Behavioral and Integrative Treatment Branch
Division of Clinical Neuroscience and Behavioral Research
National Institute on Drug Abuse
National Institutes of Health
6001 Executive Boulevard
Bethesda, MD 20892
Work Phone: (301) 442-2261
Email: kahanas@mail.nih.gov

Adeeba Kamarulzaman, M.D.
Professor of Medicine and Infectious Diseases
Departments of Medicine
Centre of Excellence for Research in AIDS
University of Malaya
Lembah Pantai
Kuala Lumpur, Malaysia 59100
Work Phone: 603 79492129
Email: deeba.kamarulzaman@gmail.com

Thomas Kerr, Ph.D.
Director
Urban Health Research Initiative
British Columbia Centre for Excellence in HIV/AIDS
608-1081 Burrard Street
Vancouver, BC V6Z 1Y6 Canada
Work Phone: (604) 806-9116
Email: uhri-tk@cfenet.ubc.ca

Jag Khalsa, Ph.D.
Chief
Medical Consequences Branch
Division of Pharmacotherapies and Medical Consequences of Drug Abuse
National Institute on Drug Abuse
National Institutes of Health
6001 Executive Boulevard
Room 4137
Bethesda, MD 20892
Work Phone: (301) 443-2159
Email: jk98p@nih.gov

Gregory Kirk, M.D., Ph.D.
Associate Professor
Epidemiology
Johns Hopkins Bloomberg School of Public Health
615 N. Wolfe Street
Baltimore, MD 21205
Work Phone: (410) 502-2038
Email: gkirk@jhsph.edu

Andrei Kozlov, Ph.D.
Director
Biomedical Center
Professor
St. Petersburg State University
8, Vyborgskaja Street
St.Petersburg, Russia 194044
Work Phone: 812 2304959
Email: contact@biomed.spb.ru

Thomas Kresina, Ph.D.
Public Health Advisor
Center for Substance Abuse Treatment
Division of Pharmacologic Therapies
Substance Abuse and Mental Health Services Administration
1 Choke Cherry Road
2nd Floor, Room 2-1075
Rockville, Maryland 20850
Work Phone: (240) 276-2713
Email: Thomas.Kresina@samsha.hhs.gov

Evgeny Krupitsky, M.D., Ph.D.
Head
Laboratory of Clinical Pharmacology of Addictives States
St. Petersburg Pavlov State Medical University
St. Petersburg, Russia
Email: kru@ek3506.spb.edu

Elizabeth Lambert, M.Sc.
Health Statsitician
Epidemiology Research Branch
Division of Epidemiology, Services and Prevention Research
National Institute on Drug Abuse
National Institutes of Health
6001 Executive Boulevard
Room 5147, MSC 9589
Bethesda, MD 20892
Work Phone: (301) 402-1933
Email: elambert@nida.nih.gov

Amy Lansky, Ph.D.
Deputy Director
Division of HIV/AIDS Prevention
Centers for Disease Control and Prevention
1600 Clifton Road, MS D-21
Atlanta, GA 30333
Work Phone: (404) 639-8663
Email: alansky@cdc.gov

Diane Lawrence, Ph.D.
Associate Director
AIDS Research Program
Office of the Director
National Institute on Drug Abuse
National Institutes of Health
6001 Executive Boulevard
MSC 9581/Room 4224
Bethesda, MD 20832
Work Phone: (301) 594-3225
Email: lawrencedi@nida.nih.gov

Jeff Levine
Press Officer
Public Information and Liason Branch
Office of Science Policy and Communications
National Institute on Drug Abuse
National Institutes of Health
6001 Executive Boulevard, Room 5221
Bethesda, MD 20892
Work Phone: (301) 594-6146
Email: levinejb@nida.nih.gov

Akiva Liberman, Ph.D.
Progam Official
Services Research Branch
Division of Epidemiology, Services and Prevention Research
National Institute on Drug Abuse
National Institutes of Health
6001 Executive Boulevard
Room 5185
Bethesda, MD 20892-9589
Work Phone: (301) 402-0808
Email: libermana@nida.nih.gov

Viviane Dias Lima, Ph.D.
Senior Statistician
HIV/AIDS Drug Treatment Program
British Columbia Centre for Excellence in HIV/AIDS
1081 Burrard Street, Room 608
Vancouver, BC, V6Z 1Y6
Work Phone: (604) 806-8796
Email: vlima@cfenet.ubc.ca

Robert Lubran, M.S., M.P.A.
Director
Center for Substance Abuse Treatment
Division of Pharmacologic Therapies
Substance Abuse and Mental Health Services Administration
1 Choke Cherry Road
2nd Floor, Room 2-1075
Rockville, Maryland 20850
Work Phone: (240) 276-2714
Email: Robert.lubran@samhsa.hhs.gov

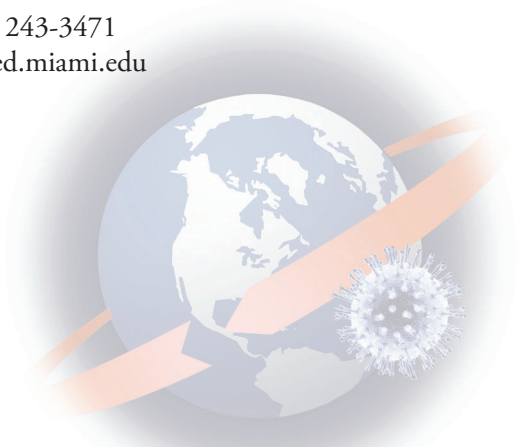
Gregory Lucas, M.D., Ph.D.
Associate Professor
Johns Hopkins Center for Global Health
Johns Hopkins University
1830 E. Monument Street
Room 435A
Baltimore, MD 21287
Work Phone: (410) 614-0560
Email: glucas@jhmi.edu

Raul Mandler, M.D.
Senior Medial Officer
Center for Clinical Trials Network
National Institute on Drug Abuse
National Institutes of Health
6001 Executive Boulevard
Bethesda, MD 20892
Work Phone: (301) 435-0645
Email: mandlerr@mail.nih.gov

Timothy Mastro, M.D.
Vice President
Family Health International
2224 East North Carolina Hwy 54
Durham, NC 27713
Work Phone: (919) 450-5358
Email: tmastro@fhi.org

A. Thomas McLellan, Ph.D.
Deputy Director
Office of National Drug Control Policy
The White House
750 17th Street NW
Washington, DC 20503
Work Phone: (202) 395-6627
Email: vwoodberry@ondcp.eop.gov

Lisa Metsch, Ph.D.
Professor
Department of Epidemiology and Public Health
University of Miami
Miller School of Medicine
1120 NW 14th Street, Suite 917
Miami, FL 33136
Work Phone: (305) 243-3471
Email: lmetsch@med.miami.edu



David Metzger, Ph.D.
Director
HIV Prevention Research
Department of Psychiatry
University of Pennsylvania
3535 Market Street, Suite 4001
Philadelphia, PA 19104
Work Phone: (215) 746-7346
Email: dsm@mail.med.upenn.edu

Greg Millett, M.P.H.
Senior Policy Advisor
Office of National AIDS Policy
The White House
Washington, DC 20502
Work Phone: (202) 456-4533
Email: gmillett@who.eop.gov

Julio Montaner, M.D.
President
International AIDS Society
Director
British Columbia Centre for Excellence in HIV/AIDS
1081 Burrard Street, Room 667
Vancouver, BC, V6Z 1Y6
Work Phone: (604)806-8036
Email: jmontaner@cfenet.ubc.ca

Emma Murphy
NIH Office of AIDS Research
Office of the Director
National Institutes of Health
5635 Fishers Lane
Bethesda, MD 20892
Work Phone: (310) 443-7520
Email: murphyee@od.nih.gov

Richard Needle, Ph.D.
Senior Public Health Advisor
U.S. President's Emergency Plan
for AIDS Relief
Department of State
2100 Pennsylvania Avenue NW
Washington, DC 20037
Work Phone: (703) 627-5448
Email: needlerh@state.gov

Jacques Normand, Ph.D.
Director
AIDS Research Program
Office of the Director
National Institute on Drug Abuse
National Institutes of Health
6001 Executive Boulevard, Room 5274
Bethesda, MD 20892
Work Phone: (301) 443-1470
Email: jnormand@mail.nih.gov

Charles O'Brien, M.D., Ph.D.
Kenneth E. Appel Professor of Psychiatry
Department of Psychiatry
University of Pennsylvania
Treatment Research Center
3900 Chestnut Street
Philadelphia, PA 19104-6178
Work Phone: (215) 222-3200
Email: obrien@mail.trc.upenn.edu

Lisa Onken, Ph.D.
Branch Chief
Behavioral and Integrative Treatement Branch
Division of Clinical Neuroscience and Beharorial Research
National Institute on Drug Abuse
National Institutes of Health
6001 Executive Boulevard, 3172
Bethesda, MD 20850
Work Phone: (301) 443-2235
Email: Lisa_Onken@nih.gov

Charles Parry, Ph.D.
Director
Alcohol & Drug Abuse Research Unit
South African Medical Research Council
PO Box 19070
7505 Tygerberg, South Africa
Work Phone: 27 21 938-0419
Email: cparry@mrc.ac.za

Marie-Capucine Penicaud
Programmes and Initiatives Officer
International AIDS Society
Avenue Louis-Casaii, 71
P.O. Box 28
CH – 1216 Cointrin
Geneva, Switzerland
Work Phone: 41 0 22-7 100 815
Email: mpe@iasociety.org

Kimberly A. Powers
Department of Epidemiology
University of North Carolina at Chapel Hill
CB 7435
Chapel Hill, NC 27599-7435
Work Phone: (505) 660-4318
Email: powersk@email.unc.edu

Sasiragha Priscilla Reddy, Ph.D.
Director
Health Promotion Research & Development Unit
South African Medical Research Council
PO Box 19070
7505 Tygerberg, South Africa
Work Phone: 27 21 938-0453
Email: priscilla.reddy@mrc.ac.za

Josiah Rich, M.D., M.P.H.
Professor of Medicine and Community Health
The Miriam Hospital
Alpert Medical School
Brown University
164 Summit Avenue
Providence, RI 02906
Work Phone: (401) 793-4770
Email: jrich@lifespan.org

Jeffrey Samet, M.D.
Professor of Medicine
Chief
General Internal Medicine
Boston University School of Medicine
801 Massachusetts Avenue
Crosstown 2
Boston, MA 02118
Work Phone: (617) 414-7288
Email: jsamet@bu.edu

Bruce Schackman, Ph.D.
Chief
Division of Health Policy
Associate Professor
Department of Public Health
Weill Cornell Medical College
402 East 67th Street
New York, NY 10065
Work Phone: (646) 962-8043
Email: brs2006@med.cornell.edu

Kate Shannon, Ph.D.
Research Scientist
British Columbia Centre for Excellence in HIV/AIDS
Assistant Professor
Department of Medicine
Division of AIDS
University of British Columbia
608-1081 Burrard Street
Vancouver, BC V6Z1Y6
Work Phone: (604) 806-9459
Email: kshannon@cfenet.ubc.ca

James Sorensen, Ph.D.
Professor
Department of Psychiatry
University of California, San Francisco
SFGH 1001 Potrero Avenue
Building 29, Suite 2100, Room 2117
San Francisco, CA 94110
Work Phone: (415) 206-3969
Email: james.sorensen@ucsf.edu

Anne Spaulding, M.D.
Assistant Professor
Epidemiology
Rollins School of Public Health
Emory University
1518 Oak Grove Drive
Decatur, GA 30033
Work Phone: (404) 727-3369
Email: ASpauld@emory.edu

Ron Stall, Ph.D.
Professor and Chair
Department of Behavioral and Community Health Sciences
Graduate School of Public Health
University of Pittsburgh
130 DeSoto Street
208 Parran Hall
Pittsburgh, PA 15261
Work Phone: (412) 624-7933
Email: rstall@pitt.edu

Steffanie Strathdee, Ph.D.
Associate Dean
Global Health Sciences
Harold Simon Professor
Chief
Division of Global Public Health
School of Medicine
University of California, San Diego
10111 N. Torrey Pines Road
La Jolla, CA 92093-0507
Work Phone: (858) 822-1952
Email: sstrathdee@ucsd.edu

Betty Tai, Ph.D.
Director
Center for Clinical Trials Network
National Institute on Drug Abuse
National Institutes of Health
6001 Executive Boulevard
Bethesda, MD 20892
Work Phone: (301) 443-2397
Email: btai@nih.gov

David Thomas, M.D., M.P.H.
Professor of Medicine
Director
Division of Infectious Diseases
Department of Medicine
Johns Hopkins Medicine
1830 East Monument Street, 4th Floor
Baltimore, MD 21205
Email: dthomas@jhmi.edu

Avelardo Valdez, Ph.D.
Professor and Director
Center for Drug and Social Policy Research
University of Houston
110 HA Social Work Building
Houston, TX 77204
Work Phone: (713) 743-8098
Email: avaldez2@uh.edu

Nora D. Volkow, M.D.
Director
National Institute on Drug Abuse
National Institutes of Health
6001 Executive Boulevard
Room 5274
Bethesda, MD 20892
Work Phone: (301) 443-6480
Email: sschloss@nida.nih.gov

Roy A. Walker
Senior Program Associate
Synergy Enterprises, Inc.
8757 Georgia Avenue, Suite 1440
Silver Spring, MD 20910
Work Phone: (240) 485-1700, ext. 124
Email: rwalker@seiservices.com

Wendee Wechsberg, Ph.D.
Senior Director
Substance Abuse Treatment Evaluation and Interventions
RTI International
3040 Cornwallis Drive
Durham, NC 27709-2194
Work Phone: (919) 541-6422
Email: wmw@rti.org

Jack Whitescarver, Ph.D.
Director
NIH Office of AIDS Research
Office of the Director
National Institutes of Health
5635 Fishers Lane, MSC 9310
Bethesda, Maryland 20892-9310
Work Phone: (301) 496-0357
Email: jackw@nih.gov

David Wohl, M.D.
Clinical Assistant Professor of Medicine
Infectious Diseases
School of Medicine
University of North Carolina at Chapel Hill
130 Mason Farm Road
2111 Bioinformatics Building
Chapel Hill, NC 27599
Work Phone: (919) 843-2723
Email: wohl@med.unc.edu

Daniel Wolfe, M.P.H.
Director
International Harm Reduction Development Program
Open Society Institute
400 W. 59th Street
New York, NY 10019
Work Phone: (212) 548-0195
Email: dwolfe@sorosny.org

Richard Wolitski, Ph.D.
Deputy Director
Division of HIV/AIDS Prevention
Centers for Disease Control and Prevention
8 Corporate Boulevard
Atlanta, GA 30329
Work Phone: (404) 639-5200
Email: RWolitski@cdc.gov

John Wong, M.D.
Professor of Medicine
Chief
Division of Clinical Decision Making, Informatics, and Telemedicine
Tufts Medical Center
800 Washington Street
Suire 302
Boston, MA 02111
Work Phone: (617) 636-5695
Email: jwong@tuftsmedicalcenter.org

Evan Wood, M.D., Ph.D.
Clinical Associate Professor
Urban Health Research Initiative
British Columbia Centre for Excellence in HIV/AIDS
608 - 1081 Burrard Street
Vancouver, BC V6Z 1Y6
Work Phone: (604) 682-2344
Email: uhri-ew@cfenet.ubc.ca

George Woody, M.D.
Professor of Psychiatry
Treatment Research Institute
University of Pennsylvania
150 South Independence Mall West
Suite 600
Philadelphia, PA 19106
Work Phone: (215) 399-0980
Email: woody@tresearch.org

Fujie Zhang, M.D.
Director
HIV/AIDS Treatment and Care
National Center for AIDS/STD Control and Prevention
Chinese Center for Disease Control and Prevention
27 Nan Wei Road
Beijing, 1000500
P.R. China
Work Phone: 8610-63039086
Email: zhang.fuji.t@gmail.com

Sheryl Zwerski, R.N.
Acting Director
Prevention Sciences Program
Division of AIDS
National Institute of Allergy and Infectious Diseases
National Institutes of Health
6700B Rockledge Drive, Room 5116
Bethesda, MD 20892
Work Phone: (301) 402-4032
Email: szwerski@niaid.nih.gov