CONFERENCE SUMMARY REPORT

AIDS 2012

XIX INTERNATIONAL AIDS CONFERENCE JULY 22 - 27
WASHINGTON DC USA

TURNING THE TIDE TOGETHER

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Stronger Together Against HIV

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AIDS 2012 Volunteers. Photo: © IAS / Deborah W. Campos – Commercialimage.net

INTRODUCTION

Diane Havlir, AIDS 2012 US Co-Chair, speaks at the Opening Sessions.
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The XIX International AIDS Conference (AIDS 2012) returned to the USA after 22 years amidst a backdrop of tremendous optimism that an end to the HIV epidemic is possible, tempered with recognition that many years of hard work remain ahead.

Over 23,000 participants gathered in Washington, D.C., to attend the biennial conference, as well as dozens of affiliated events and Satellite Sessions (see sidebar: AIDS 2012 Statistics). Speakers and participants embraced the conference theme, *Turning the Tide Together*, as an urgent call to act on recent scientific advances in HIV treatment and biomedical prevention, the momentum for an HIV vaccine and cure, and continuing evidence of the ability to scale up effective interventions in the most-needed settings.

AIDS 2012 STATISTICS

- 17,066 delegates
- 11,725 non-USA participants
- 851 scholarship recipients
- 1,904 journalists
- 991 volunteers
- 183 countries represented
- 194 abstract and non-abstract-driven sessions
- 60 workshops.

People living with HIV (PLHIV) spoke at a broad cross-section of sessions, including plenaries. AIDS 2012 featured the largest Global Village at an International AIDS Conference, with over 190,000 square feet (18,000m^2) and 265 events. The conference garnered significant global media coverage, and participants utilized technology and social media to maximize the impact of their participation.

This report provides a concise summary of key findings and lessons learned from AIDS 2012 for those working in HIV and related fields, and for policymakers worldwide. The conference's programme focused on using recent scientific developments to scale up treatment and biomedical prevention efforts, identifying and addressing the challenges to discovering a cure for HIV, and addressing stigmatization, discrimination, and poverty. Highlights within each of the three conference programme areas – Science, Leadership and Accountability, and Community – are presented, along with an analysis of the implications of conference outcomes on HIV practice, policy and research. A formal evaluation of AIDS 2012 based on delegate feedback is underway. Findings will be available in the AIDS 2012 Evaluation Report, slated for release in December 2012, and available on the International AIDS Society (IAS) and conference websites (www.iasociety.org and www.aids2012.org, respectively).

This report is purposely short, and focuses on the most important themes and stories from AIDS 2012. We encourage readers to broaden their understanding of the conference by using the many hyperlinks provided in the report, particularly the links to session pages on the AIDS 2012 Programme-at-a-Glance http://pag.aids2012.org, which provides video recordings, rapporteur summaries, and presentation slides (when available) for all plenary sessions, as well as many other sessions and workshops. The Programme-at-a-Glance also provides links to webcasts produced by the Kaiser Family Foundation. The AIDS 2012 website www.aids2012.org is a rich source of research, policy and programmatic information.

The report is structured as follows:

EXECUTIVE SUMMARY

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- Tracks A, B and C: Basic Science, Clinical Science and Epidemiology and Prevention Science
- Track D and E: Social Science, Human Rights and Political Science and Implementation Science, Health Systems and Economics

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- Achieving an AIDS-Free Generation
- Maintaining Political Momentum and Country Ownership Inclusion of Vulnerable Populations in Setting Policy

COMMUNITY

- Criminalization of HIV and Marginalized Groups
- HIV Entry Barriers for Sex Workers and people who use drugs
- Human Rights and Biomedical Prevention Strategies
- Alternative Funding Sources
- Youth Leadership
- Communities and Individuals Driving Change

AIDS 2012 Entrance Hall, Walter E. Washington Convention Center.
Photo: © IAS / Ryan Rayburn – Commercialimage.net

EXECUTIVE SUMMARY

AIDS 2012 registration area. Photo: © IAS / Ryan Rayburn – Commercialimage.net

SCIENCE

TRACKS A, B AND C: BASIC SCIENCE, CLINICAL SCIENCE AND EPIDEMIOLOGY AND PREVENTION SCIENCE

The two-day pre-conference symposium "Towards an HIV Cure" unveiled a research strategy for progressing through the complex questions that scientists must answer before HIV in patients' bodies can be suppressed to the point where HIV no longer poses a threat requiring constant antiretroviral therapy. The strategy focuses on two areas: 1) further characterization of the so-far untreatable HIV reservoirs and 2) elucidation of the means by which "elite controllers" manage to keep their HIV infections at very low levels even when not on antiretroviral therapy (ART).

In his plenary session, Javier Martinez-Picado (AIDS Research Institute, Barcelona, Spain) laid out a three-step research programme that set the stage for much of the research presented in Track A: 1) review basic science to understand the cellular, viral and immunological mechanisms that support HIV persistence; 2) develop new assays and experimental models to tackle viral reservoirs; and 3) investigate new therapeutic agents and immunological strategies to achieve viral remission in the absence of ART.

Several studies examining the impact of various interventions on viral reservoirs were presented. Charline Bacchus (French National Agency for Research on AIDS and Viral Hepatitis (ANRS)) presented data on a set of 11 persons (part of the VISCONTI cohort) treated with ART within 10 weeks of acquiring HIV. Six years after interruption of treatment, these 11 patients possess an extremely low reservoir of HIV in their cells, similar to that of "elite controllers." In another presentation, Timothy Heinrich (Harvard Medical School) described the unexpected long-term reduction in peripheral blood HIV-1 reservoirs in four patients with ART-suppressed HIV who had received allogeneic hematopoietic stem cell transplants with HIV-susceptible cells.

Geeta Rao, Linda Scruggs, Chewe Luo, Barton Haynes Duke, Joseph Essombo and Mabel Bianco at the AIDS 2012 Wednesday Plenary Session.
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According to research presented by the AIDS Clinical Trials Group, a human papillomavirus (HPV) vaccine designed to protect against four high-risk HPV genotypes had strong activity in a trial of young and middle-aged HIV-positive women in the USA, Brazil and South Africa. Investigators from the Adolescent Medicine Trials Network presented data from a second HPV trial that they believe supports the vaccination of young HIV-positive women.

Two additional studies presented at AIDS 2012 contained potentially significant treatment implications. Three newer antiretrovirals-the integrase inhibitors raltegravir and dolutegravir and the nonnucleoside etravirine – had good antiviral activity in three studies of children and adolescents taking failing regimens. In HPTN 052, the first trial that randomised HIV-positive people to start ART above 350 or below 250 CD4 cells/mm^3, earlier ART significantly lowered incidence of AIDS-related diseases and tuberculosis. HPTN 052 investigators proposed that "the combined treatment and prevention benefits of ART support early initiation" of treatment.

From a treatment-as-prevention perspective, HPTN 052 established the principle that treating HIV-positive people at a higher CD4 count lowers the risk that they will transmit the virus to steady sex partners. Several reports offered further analysis of HPTN 052, and of related studies of the test-and-treat strategy, which calls for expanded HIV testing and immediate treatment of everyone who tests positive. Some of this research raised questions about how effective test-and-treat will be in practice, rather than in a carefully controlled trial.

AIDS 2012 offered results of research on two simple circumcision methods that require less expertise and time than traditional methods that require surgical staff and operating room time. Studies on the Shang Ring and PrePex methods offer evidence that circumcision can be completed safely and effectively after brief training of non-physician professionals. These simpler circumcision procedures could help lower HIV incidence in high-prevalence countries with a shortage of trained physician surgeons.

TRACK D AND E: SOCIAL SCIENCE, HUMAN RIGHTS AND POLITICAL SCIENCE AND IMPLEMENTATION SCIENCE, HEALTH SYSTEMS AND ECONOMICS

Several presenters examined the correlation between a country's level of development and its prevalence of HIV. James Hargreaves (London School of Hygiene and Tropical Medicine, London, U.K.) showed that HIV is initially more prevalent in higher socioeconomic strata; however, as the epidemic evolves, less educated sectors of the population eventually are afflicted with higher HIV rates. Heather Worth (University of

Elly Katabira, AIDS 2012 International Chair at the AIDS 2012 Symposium Session "Improving Effectiveness and Efficiency in the HIV response".
Photo: © IAS / Steve Shapiro – Commercialimage.net

New South Wales, Sydney, Australia) reported that reduced corruption was the governmental factor with the strongest correlation with ART use. Craig Phillips (University of Ottawa, Ottawa, Canada) presented research findings that specifically contradicted the idea that inequality in wealth distribution has a major influence on low treatment adherence among a country's residents. Rather, researchers found that a country's overall democracy ranking, HIV criminalization and social capital score were the three variables correlated with improved adherence.

The impact of stigmatization of men who have sex with men (MSM), particularly young MSM, was made clear by the results of a global telephone survey of MSM presented by Glenn-Milo Santos (University of California San Francisco, San Francisco, USA). Perceived negative social attitudes to homosexuality were the greatest predictor of young MSMs' self-reported lack of HIV prevention services. Additional surveys in Malawi and India found widespread fear among MSM of disclosing their sexuality and the associated negative effect on their well-being and increased rates of HIV transmission.

AIDS 2012 attendees heard that violence has an ill effect on women's health in both developed and less-developed countries. The Women's Interagency HIV Study (WIHS) found that women in its cohort (1,642 HIV-positive and 580 HIV-negative) report partner violence at about the same rate (36%) as Indian surveys of married women. In Northern Uganda, years of warfare and forced evacuations have led to a large population of female sex workers.

Researchers from the University of British Columbia (Vancouver, Canada) and The AIDS Support Organization (Gulu, Uganda) reported that these women are subject to an increasing law-enforcement clampdown. At the same time, their HIV prevalence soared. The police pursuit of intravenous drug users has effects

similar to the criminalization of sex workers. University of British Columbia researchers along with Thai activist groups undertook a survey among Thai injection drug users that was similar to the one among northern Uganda sex workers.

Irene Hall (Centers for Disease Control and Prevention (CDC), Atlanta, USA) presented a government-sponsored report on the demographic factors linked to real-world response to ART. Major differences in treatment access in the USA and other countries revolve around race and age. Age differences in the percentage of PLHIV with viral suppression reflect the challenges faced by two distinct groups: adolescents and those over 50. Adolescents and young adults tend to be alienated from the established adult world, while older PLHIV often face isolation and depression.

Many of the presentations and discussions in Track E focused on the growing international acceptance that there is one optimum world standard for HIV treatment. On the eve of AIDS 2012, the World Health Organization (WHO) issued a position paper, The Strategic Use of Antiretrovirals to Help End the HIV Epidemic. At the conference, Anthony Harries (International Union Against Tuberculosis and Lung Disease, Paris, France) summarized WHO's evolution and current position on HIV treatment access. The WHO is advising (though not yet officially recommending) that treatment should be available to all HIV-positive persons who belong to specific high-risk populations regardless of CD4 count. The WHO envisions further steps that would lead to a universal "test and treat" strategy in which anyone could be put on treatment as soon as they receive a positive HIV test result. This goal hinges on the dramatic results from the HPTN 052 trial. The WHO is also advocating an expansion in ART to prevent mother-to-child transmission.

A number of conference presentations considered how to meet the challenge of increasing ART coverage. Yogan Pillay (National Department of Health, Pretoria, South Africa) in his plenary address argued that only increased efficiencies will provide the (financial) foundation for universal access. Countries must restructure their HIV services, investing available HIV funds in programmes that are most effective in reducing HIV mortality and incidence.

Also, the increasing calls for earlier treatment means that developing countries will be dependent on international funding for the foreseeable future despite recent gains in their own budget allocations for HIV care. Several presenters examined the economic implications of starting ART at various stages of infection, including beginning treatment immediately after diagnosis, regardless of CD4 count. There was also significant discussion about the economic benefits of treatment-as-prevention. Till Bärnighausen (Harvard School of Public Health, Boston, USA) made the case that combining high ART coverage under current guidelines and high circumcision coverage would provide more or less the same reduction in HIV as a treatment-as-prevention approach but would be much less expensive.

Demonstration at AIDS 2012. Photo: © IAS / Ryan Rayburn – Commercialimage.net

LEADERSHIP AND ACCOUNTABILITY

There was a great deal of optimism at AIDS 2012 that HIV as an epidemic could be controlled within a generation. Despite that optimism, the fact that a cure for HIV is still not within sight was a key topic at the conference. So too, the financial and logistical challenges of achieving an AIDS-free generation were the subject of many sessions.

The concept of country ownership was a recurring theme throughout AIDS 2012, as was the reality that affected countries need to collaborate with international donors to make meaningful use of increasingly scarce resources. There needs to be a focus on greater transparency, accountability, and efficiency. It was also acknowledged that country ownership will require new funding sources for resource-poor nations. Several speakers made the case for the continued commitment of developed nations. Numerous sessions addressed the role the private sector must play in a sustained effort to end AIDS.

Many presenters criticized USA immigration policy denying sex workers and people who use drugs entry to the USA and called for the USA to change this policy. Speakers implored leaders, especially those in Africa, to include MSM in national HIV strategies. There was consensus among conference participants that a real need exists to fight prejudice, stigma, discrimination, exclusion, and criminalization.

The involvement of youth in setting policy agendas was discussed at AIDS 2012, as was the role of faith-based organizations, particularly in developing nations. The use of social media as an accountability tool was a topic at a number of sessions, and several speakers pressed for the inclusion of people with disabilities in national strategic plans.

COMMUNITY

The AIDS 2012 Community Programme reaffirmed human rights as the central vehicle to end the HIV epidemic and included sessions examining the barriers to implementing effective interventions and strategies for overcoming them. Among those challenges are the criminalization of HIV and marginalized groups, and related issues of stigma and discrimination.

USA entry restrictions on sex workers and people who use drugs, and their inability to fully participate in AIDS 2012, provided a stark example of the barriers and challenges facing both groups. These challenges were discussed throughout the conference and were the subject of several protests by activists. During the week of the conference, more than 500 sex workers from 41 countries attended an official conference hub in Kolkata, India, while drug users participated in a pre-conference forum in Kiev, Ukraine.

Effective biomedical strategies were recognized as showing great promise in preventing onward transmission and reducing community viral load, but the need to protect and strengthen human rights was a recurring theme in relation to how these strategies would need to move forward. There was a tremendous amount of urgency at AIDS 2012 to discuss developing new, on-going and stable funding sources for global HIV and AIDS initiatives. Beyond funding schemes, speakers and delegates also called for governments and drug manufacturers to ensure that patent laws and restrictive pricing do not inhibit the effective global rollout of life-saving medications.

Young people are key to moving towards the goal of an AIDS-free generation and a number of sessions dealt with the issues they face both in terms of living with HIV and seeking to prevent new infections.

While global and national responses are key to removing legal and structural barriers, the need to work for change at the personal level is equally crucial. Several sessions showcased tools to advocate for this change and for the greater involvement of people living with HIV and key populations at higher risk. Community members led and participated in many conference sessions, including discussions around the Black Diaspora, improving the number and quality of HIV healthcare workers, and building a political voice to address sexual reproductive health and rights for women living with HIV.

Demonstration at AIDS 2012.
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SCIENCE

Françoise Barré-Sinoussi, IAS President, speaks at the "Towards an HIV Cure" Press Conference.

TRACK A: BASIC SCIENCE

THE LONG ROAD TO A CURE

Present-day ART has proven highly successful, increasing life expectancy to near normal levels, as Anthony Fauci of the National Institute of Allergy and Infectious Diseases (Bethesda, USA) pointed out in one of AIDS 2012's early plenary sessions[1]. Still, ART has serious limitations. It can suppress HIV to undetectable plasma levels, but residual latent HIV remains in a small population of resting T-cells. This silent HIV (present in about one in a million cells) begins to replicate when the host cell activates. If a person with HIV ever stops his or her suppressive ART regime, this reservoir of HIV is the source of a rapid rebound in viral load. ART's limitations thus obligate patients to deal with life-long issues related to ART toxicities and cost as well as continued morbidity due to chronic immune activation. If patients' adherence ever falters and viral replication resumes, then they have additional HIV-related illnesses to confront, and may transmit the virus to others.

Researchers are beginning to address this conundrum. The two-day pre-conference symposium "Towards an HIV Cure" unveiled a strategy for progressing through the complex research questions that need answers before we can suppress HIV in patients' bodies to the point it is no longer a threat that requires constant management[2]. The research strategy focuses on advances in two areas: 1) further characterization of the so-far untreatable reservoirs and 2) elucidation of the means by which the "elite controllers" manage to keep their HIV infections to very low levels even when not on antiretroviral therapy.

Sharon Lewin, Rowena Johnston, Steven Deeks, Françoise Barré-Sinoussi, Mark Harrington and Michel Sidibe at the Towards an HIV Cure press conference.

These two areas are critical to the two types of possible cure – eradication, in which the virus is eliminated from the body, and functional cure, in which residual HIV remains but is held in check by the immune system. A plenary address at AIDS 2012 by Javier Martinez-Picado (AIDS Research Institute, Barcelona, Spain) on the "cure agenda" reviewed these issues and set the stage for much of the research presented as part of Track A[3]. In line with the cure strategy discussed at the pre-conference symposium, Martinez-Picado laid out a three-step research programme: 1) review basic science to understand the cellular, viral and immunological mechanisms that support HIV persistence; 2) develop new assays and experimental models to tackle viral reservoirs (tissues and cellular sources) in long-term ART-treated individuals; and 3) investigate new therapeutic agents and immunological strategies to achieve viral remission in absence of ART.

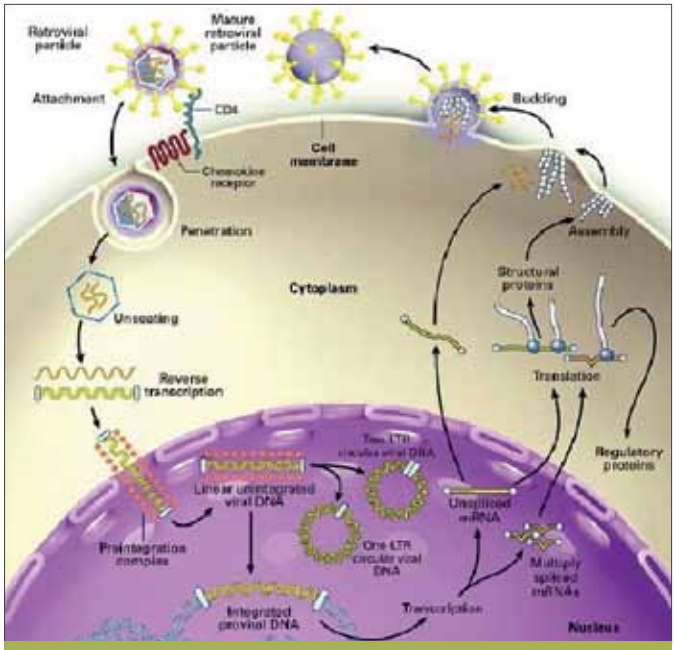
FERRETING OUT THE HIDDEN RESERVOIRS

It would be extremely useful if we could recognize patient cells harbouring latent HIV infections. Since these cells produce no HIV virions or even viral proteins, neither the human immune system nor current antiretroviral treatments are able to target these specific cells. Fabio Romerio (University of Maryland, Baltimore, USA) described the in vitro model that his lab has developed to study this question[4]. The group utilizes dendritic cells to activate naive CD4+ T-cells in cell culture, which are then susceptible to the HIV introduced into the culture[5]. The cells, which have developed a memory T-cell phenotype, are then separated out and restored to a resting state for several weeks. They then lack expression of activation markers and show no signs of proliferation or viral replication. The infected cells are still distinguishable by the slowly degrading presence of intracellular HIV p24 antigen, and a messenger RNA assay reveals substantial differences between the resting cells depending on their HIV status. The latently infected cells in particular have downgraded their cell activation and metabolic activity (while upregulating genes that protect against cell death).

This apparent defence may present a hurdle to therapies that attempt to activate the cells in the presence of ART in order to eliminate the pool of latent HIV. Such drugs' lack of activity was the subject of a recent report[6]. However, the Romerio group found considerable differences in cell surface marker expression – which involves 33 different proteins – that distinguish the latently infected cells and provide a mechanism for therapy. One such marker validated by the researchers is CD2.

Before research concentrates on mechanisms to kill cells exhibiting CD2 above a certain threshold density, it is worth remembering that the pool of latent HIV probably includes several different cell types. HIV integration with nuclear DNA fails 90-99% of the time. The general view is that unintegrated DNA within the cell has reached a dead-end in its lifecycle, but this is not necessarily so[7]. A presentation by David Levy (New York University, New York City, USA) described a small pool of resting CD4+ T-cells containing replication-competent unintegrated proviral DNA existing in a

The HIV Lifecycle Includes Integrated and Unintegrated Proviral HIV DNA



Source: Furtado MR et al. N Engl J Med 1999;340:1614-1622.
Diagram: via Helga Hofmann-Sieber, T UAA0302, slide 2

circularized, or episomal, form in the cells' nucleus[8]. The resulting viral production, amounts to about 10% that of integrated HIV DNA. This source of virus is not inhibited by an integrase inhibitor like raltegravir. On the contrary, Levy's in vitro results suggest that integrase inhibitors enhance the presence of unintegrated latent HIV proviral DNA.

Raltegravir is frequently added to ART in human studies of treatment intensification. Those studies generally report failure to reduce HIV levels to a greater extent than standard three-drug regimens. Clinical studies indicate further that long-term raltegravir intensification does not reduce either plasma HIV RNA or cellular proviral DNA levels (both total and integrated)[9, 10]. Accumulation of replication-competent episomal DNA might be part of the reason that raltegravir intensification is not effective, but reports differ as to whether this accumulation occurs even on a temporary basis.

At AIDS 2012, Timothy Schacker (University of Minnesota, Minneapolis, MN) mentioned in his symposium address the preliminary results of a study that he and colleagues are conducting on differences between tissues in the virologic response to initiating standard three-drug ART[11, 12, 13]. The majority of patients analysed so far exhibited an increase in total and episomal unintegrated HIV DNA in the first six months of therapy. This sign of residual replication occurred most prominently in lymph nodes. The researchers related it to the very low ART levels achieved in lymphoid tissue cells relative to cells in the blood.

VIRAL ERADICATION BY ELIMINATING HIV RESERVOIRS

Once the HIV latent reservoir is fully characterized, it will be possible to formulate cure strategies that eliminate this viral sanctuary. Even now, researchers are moving in that direction, testing proposed therapies that activate quiescent genes. One of the mechanisms involved in these studies is histone deacetylation (HDAC), which keeps genes tightly wound around the histone protein that forms chromosomes' structural core. Adding acetyl groups to certain points on the histone rods allows the surrounding DNA to unravel, leading to gene transcription and expression (see figure). HDAC inhibitors that promote this acetylation are already an approved treatment for certain cancers.

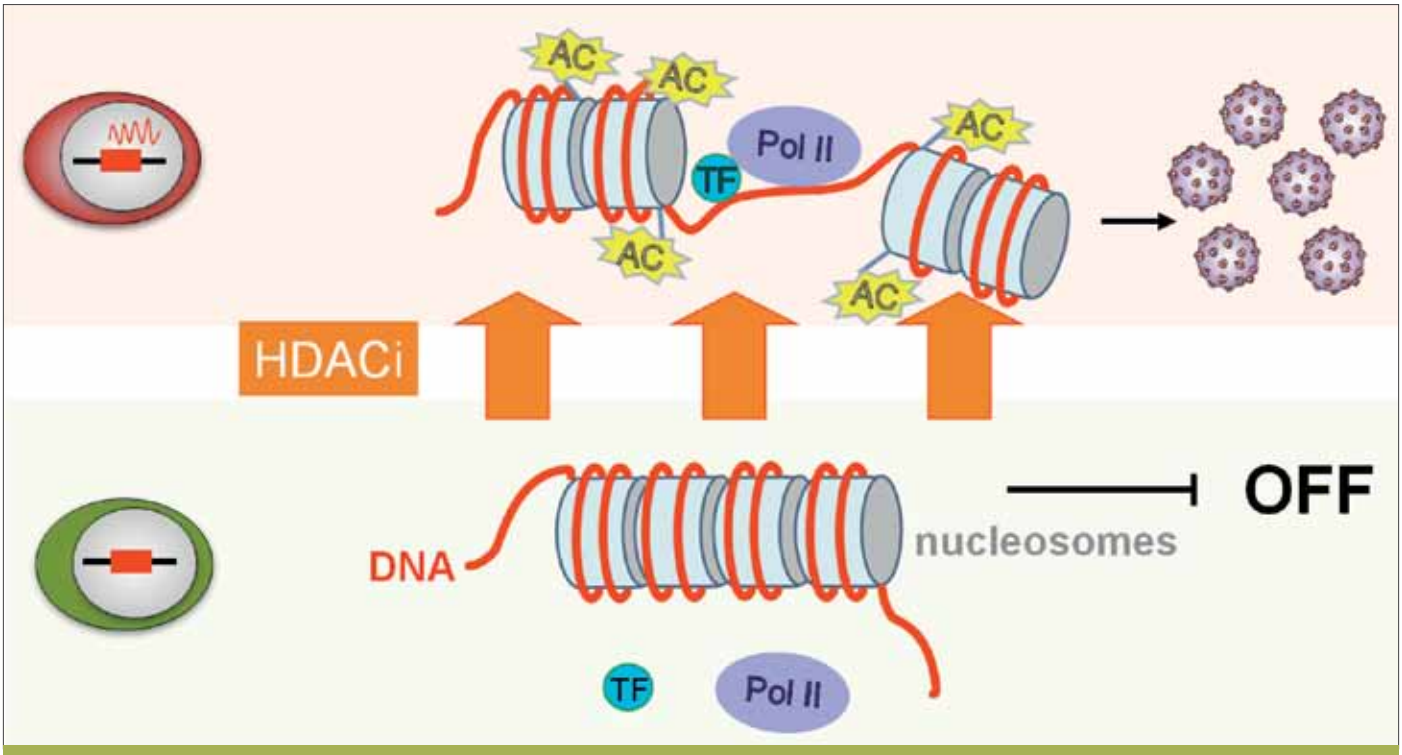
An AIDS 2012 late-breaker abstract presented by Jay Lifson (National Cancer Institute, Frederick, USA) described the use of one HDAC inhibitor, vorinostat, in SIV-infected rhesus macaques[14]. Six macaques were treated with highly suppressive ART starting four weeks after infection and then given four three-week cycles of vorinostat starting 22 weeks later. Vorinostat had no consistent effect on plasma or cell-associated SIV RNA. The effect on histone acetylation was itself variable. Conversely, ex vivo cultures of the monkeys' cells in the presence of vorinostat enhanced the induction of HIV activity. This was a sign, the researchers argued, that an insufficient amount of vorinostat was reaching the cells in vivo. It could also relate to the findings of the Romerio group described above concerning the exceptionally quiescent nature of latently infected resting T-cells.

In contrast to the macaque results, a newly reported preliminary study with eight human volunteers observed that a single vorinostat dose can increase cellular acetylation and HIV RNA expression in resting CD4+ T-cells both in vivo and ex vivo[15]. It should be noted that those volunteers were selected through a screening assay that revealed their latent HIV's sensitivity to vorinostat.

LEARNING FROM NATURAL CONTROLLERS OF HIV INFECTION

Another major objection to utilizing HDAC inhibitors as a single agent for HIV eradication arose in a widely discussed study published last winter.[16] That in vitro study used vorinostat to activate latent HIV in resting CD4+ T-cells taken from patients on suppressive ART. Successfully activating latent HIV did not lead to cell death, which would be necessary to completely eliminate the latent HIV pool. Even the introduction of autologous cytolytic T lymphocytes (CTLs) into the cell culture did not lead to the killing of infected cells. Efficient cell killing required prior stimulation of these CD8+ CTLs with HIV antigens to enrich the HIV-targeting population.

HDAC Inhibitors turn HIV genes "on"



Source: Furtado MR et al. N Engl J Med 1999;340:1614-1622. Diagram: via Helga Hofmann-Sieber,T UAA0302, slide 2.

The role of HIV-specific CD8+ CTLs in viral control has been well documented in the literature, especially in the case of "elite controllers"[17]. These rare untreated persons maintain very low HIV levels indefinitely, usually with normal CD4+ T cell counts. At AIDS 2012, Cristian Apetrei (University of Pittsburgh, Pittsburgh, USA) described the use of rhesus macaques infected with African green monkey SIV (SIVagm) as a model of elite control [18]. After severe primary infection with SIVagm, the macaques reduce their plasma HIV RNA levels to less than 1 copy/mL and regain normal immune cell populations and function. However, depleting these animals of their CD8+ cells results in a rebound in infectious HIV genetically similar to the initially acquired SIV. This result indicates the presence of a latent viral reservoir formed early in the disease process that is held in check by CTLs.

Elite controllers in humans with strong anti-HIV CTL responses frequently have particular HLA class-1 alleles associated with protection against disease progression, such as HLA B*57 and B*27. There are many nonprogressors without such genes, however. This observation has led to renewed interest in studying antibody responses to better account for elite controllers' viral suppression. A study presented at AIDS 2012 by Martyn French (University of Western Australia, Perth, Australia) described the IgG antibody makeup of 32 HIV controllers (untreated HIV RNA levels from nearly undetectable up to 2,000 copies/mL) compared to that of 21 ART-naïve HIV progressors[19].

The Perth researchers found that controllers produced IgG1 or IgG2 antibodies to one or more HIV core antigens (p17, p24) more often than non-controllers (75% vs. 28.6%, p=0.0016, for IgG1 and 22% vs. 0%, p=0.034, for IgG2). Anti-HIV Env (gp140) IgG antibodies did not differ between the two groups, although antibody-dependent cellular cytotoxicity was considerably higher among the controllers. When the comparison was confined to controllers with or without protective HLA class-1 alleles, the study found that IgG2 antibodies to core antigens were more common in the controllers (57%) than patients with these alleles (16.5%) (p=0.026). The IgG2 antibodies were still less in evidence among the progressors. The researchers hypothesized that IgG2 antibodies confer a more effective immune response against HIV due to their special affinity to plasmacytoid dendritic cells. Besides having the ability to present antigen to T-cells, plasmacytoid dendritic cells are large producers of interferon-α and -λ. Hence, they stimulate innate as well as adaptive immunity.

Another presenter to describe heightened antibody production in HIV controllers was Nuria González (Instituto de Salud Carlos III, Madrid, Spain)[20]. Her group compared broadly neutralizing antibodies in long-term nonprogressors (LTNPs) and persons with normal HIV progression. Broadly neutralizing antibodies block cellular entry to a wide variety of HIV strains and thus reduce the chances of HIV escape from immune control.

The 129 LTNPs had median plasma HIV RNA of 87 copies/mL and a CD4+ T-cell count of 802 cells/mm^3 whereas the progressors had viral and CD4 levels of 10,2412 and 567, respectively. 9.3% of the LTNPs versus 3.7% of the progressors were producing broadly neutralizing antibodies. In both LTNPs and progressors, these antibodies most frequently had affinity with the sites on the viral envelope: the CD4 binding site on gp120, gp120's V3 loop and a gp41 region playing a critical role in virus-cell fusion. The V3 loop neutralizing antibodies were more abundant in the LTNPs.

There is some indication that early treatment can sometimes mimic the conditions seen in elite controllers, reducing the latent HIV reservoir and giving the immune system the upper hand over the virus. A study of the French VISCONTI cohort[21] presented by Charline Bacchus (Hôpital Pitié-Salpêtrière, Paris, France) described a set of 11 persons treated with ART within ten weeks of acquiring HIV[22]. They continued treatment for a median 3.04 years (1-7.7) and have been off treatment a median 6.6 years (4-9.6) with median plasma HIV RNA levels of 1.7 log copies/mL (<1.7-2.46) at last visit. (Their median pretreatment HIV RNA level was 5.0 log10 copies/mL.) These "post-treatment controllers" (PTC) were compared to a group of eight never-treated elite controllers and eight HIV+ persons with HLA B*57 or B*27 alleles (including four of the elite controllers).

Among the PTC, latent HIV infection within resting memory CD4+ T-cell subsets occurred at frequencies similar to those of elite controllers. Depending on the T-cell subset, the PTC latent HIV pool was less than or equal to that of the comparison group with the protective HLA alleles. However, there were differences between the population size of the resting T-cell subsets in the PTC and elite controller groups.

Since the PTCs had detectable plasma HIV RNA and their latent HIV reservoirs could be induced to replicate, they clearly had not experienced viral eradication. The question is whether the PTCs represent a functional cure or are simply a group that would have become natural elite controllers if they had not received early ART. The researchers argued for the functional cure given that these patients made up 15% of the early treatment study population. This is a much higher frequency than that of elite controllers in the overall population with HIV. In addition, the PTCs were distinguished by their general lack of protective HLA alleles and a skewed resting CD4+ T-cell population.

IN THE AFTERMATH OF THE "BERLIN PATIENT"

While waiting for further data from the VISCONTI cohort, The "Berlin Patient" (Timothy Ray Brown) remains the sole patient whose HIV cure is generally accepted[23]. Brown received a hematopoietic stem cell transplant (HSCT) from a donor lacking functional genes for the CCR5 receptor that HIV can use along with CD4 to enter cells. The reconstituted CD4+ T-cell population was therefore impervious to the main HIV population in the recipient's body, but it should have been infectable by any minority CXCR4-using HIV variants present. According to genotype-based prediction algorithm, 2.9% of the pretransplant HIV in the Berlin patient's body should have been able to use CXCR4 instead of CCR5 as a coreceptor. One of the conference presentations explained why these variants failed to take hold after the transplant[24].

Coreceptor prediction is an imprecise science. In vitro culture studies found that Brown's predicted CXCR4-using HIV variants were in fact completely dependent on CCR5 for cell entry. They could not replicate in the descendants of the transplanted stem cells any more than Brown's dominant HIV variants. The inability of the surviving post-transplant HIV to switch coreceptor is another indication of the height of the poorly characterized barriers to such a switch, which normally occurs only in about half the patients with HIV and usually only during advanced disease[25].

AIDS 2012 Kick-Off Session.
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AIDS 2012 Opening Session, Florence Uche Ignatius and her daughter Ebube Francais Taylor.
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This study is further reassurance for the efforts already taking place to simplify the cure strategy followed in the Berlin patient's case so that it can come into general use. Timothy Heinrich (Harvard Medical School, Boston, USA) and his colleagues are now following four patients with ART-suppressed HIV who required allogeneic HSCTs to combat their refractory lymphomas and leukemias[26]. Long-term data is now available on two of these patients.

An important point is that the patients received reduced intensity conditioning to limit their own immune cell population prior to the transplant. The relatively low toxicity from this conditioning allowed the patients to remain on ART without interruption, unlike Brown. Also unlike Brown, the patients received donor cells with normal CCR5 genes. After about a year, the transplanted cells had completely supplanted the patients' original peripheral blood mononuclear cells (PBMCs). Viral outgrowth assays were completely negative for HIV after two years in one case and after 3.5 years in the other. Follow-up is continuing, and the patients remain on ART. Only a treatment interruption could answer the question of whether HIV eradication or a functional cure has occurred.

Two factors may have helped these patients reach negligible or null viral levels. One is that their continued use of suppressive ART protected the donor cells from becoming infected.

Another is that they both experienced extensive graft versus host disease episodes after their transplants. In a manner analogous to the graft versus leukemia effect that occurs with such transplants, the attack of the donor cells on the genetically different host PBMCs may have killed off the remainder of the native immune system, including the cells latently infected with HIV.

It is difficult to see how any hematopoietic stem cell strategy lacking a graft versus host effect would eradicate HIV infection, though it might lead to a functional cure. For example, engineering patient stem cells to create HIV-specific CTLs, has been subject to reports at AIDS 2012 and elsewhere [27, 28]. This technique might lead to suppression of any HIV that spontaneously emerges from latency. It could support therapies that stimulate latent virus but could never purge latent HIV on its own.

The same can be said of methods that defend PBMCs from HIV infection without actively pursuing latent virus. Helga Hofmann-Sieber (Heinrich Pette Institute – Leibniz Institute for Experimental Virology, Hamburg, Germany) reported results of transfecting cells with the gene for an enzyme dubbed Tre-recombinase that excises part of the long terminal repeats at each end of the HIV proviral DNA [29]. For safety reasons, the gene for Tre-recombinase includes a promoter region requiring stimulation by HIV Tat protein. Tre-recombinase therefore is expressed only in cells with active HIV infection and has no activity in latently infected cells.

When a humanized mouse model of HIV infection is engrafted with Tre-recombinase transfected CD4+ T-cells or hematopoietic stem cells, the presence of the enzyme reduces the number of infected cells by about one log in the 12 weeks after infection (compared to Tre-recombinase-negative control mice). Cells actively producing HIV p24 protein are essentially eliminated, possibly to a greater extent with the transfected stem cells.

Cell-permeable versions of the Tre-recombinase enzyme have been created that have anti-HIV activity in vitro [30]. These pharmaceutical versions could directly contribute to viral eradication strategies by excising active and quiescent provirus alike. Once safety is ensured and potency improved, a Tre-recombinase-type drug could become a curative agent suitablefor widespread use.

Bertrand Audoin, Elly Katabira, Diane Havlir, Michel Sidibe, Barbara Lee and Mark Dybul at the AIDS 2012 opening press conference.
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TRACK B: CLINICAL SCIENCE

HPV VACCINE HAS STRONG ACTIVITY IN HIV-POSITIVE WOMEN

A human papillomavirus (HPV) vaccine designed to protect against four high-risk HPV genotypes had strong activity in trials of young HIV-positive women in the USA[1] and young and middle-aged women in the USA, Brazil and South Africa.[2]

The quadrivalent vaccine is effective in preventing HPV infection in young women in the general population, but its activity in HIV-positive women was unknown until results of two studies presented at AIDS 2012.[1,2] HIV-positive women and men run an increased risk of HPV infection and progression to HPV-related cancers, including invasive cervical cancer and anal cancer. A systematic review presented at AIDS 2012 determined that HPV infection doubles the risk of HIV acquisition in women and men.[3]

The trial in young women involved 99 women from 16 to 23 years old in the Adolescent Medicine Trials Network (ATN).[1] Women received the vaccine that protects against HPV types 6, 11, 16, and 18 on study day one and at weeks eight and 24. Sixty-nine women had never taken antiretroviral therapy (ART) or had not taken ART in six months, while 30 women had taken ART for at least six months and had two viral loads below 400 copies/mL. ATN researchers compared vaccine responses in these women with responses in 276 HIV-negative women who received the same vaccine earlier in Brazil, Europe and the USA.

Most women in both trials were negative for HPV-6, 11, 16 or 18 when the studies began, and the geometric mean titer (GMT) and seroconversion analyses involved only women negative for those types at baseline.

When comparing GMT antibody responses against the four HPV types in women on ART and historical controls, the researchers found no significant differences (Table 1). In women off ART, GMTs against HPV 16 and 18 were significantly lower than in historical controls but still relatively high. Seroconversion rates (defined as GMTs >20, 16, 20 and 24 mMu/mL against HPV-6, 11, 16 and 18) were 100% for all historical controls and all women on ART for all HPV types. Seroconversion rates for women off ART were 90% or higher for each HPV type. Side effects were mild and usually limited to injection sites.

The second HPV vaccine trial, ACTG A5240, enrolled 130 adolescents and women from 13 to 45 years old with a CD4 count above 350 cells/mm^3, 95 participants with 200 to 350 cells/mm^3 and 94 with 200 cells/mm^3 or fewer.[2] The AIDS 2012 report involved participants in the first two groups, 196 from the USA and 29 from Brazil or South Africa, who received the vaccine on the same schedule as in the ATN trial.

Defining seroconversion as in the ATN trial, ACTG investigators recorded high seroconversion rates and GMTs (Table 1) in both study groups:

CD4 count above 350 *cells/mm^3*

- HPV-6: seroconversion rate 96%
- HPV-11: seroconversion rate 97.6%
- HPV-16: seroconversion rate 98.4%
- HPV-18: seroconversion rate 90.7%

CD4 count 201 to 350 *cells/mm^3*

- HPV-6: seroconversion rate 100%
- HPV-11: seroconversion rate 98.3%
- HPV-16: seroconversion rate 98.2%
- HPV-18: seroconversion rate 84.3%

No grade 3 or 4 adverse events were judged related to the HPV vaccine.

ATN investigators believe their results support vaccination of young HIV-positive women. The ACTG researchers think their data suggests that most HIV-positive women would benefit from HPV vaccination. The USA Centers for Disease Control and Prevention (CDC) recommends HPV vaccination for all teen girls and women through age 26 who did not get all three doses of the vaccine when they were younger.[4]

Table 1. Post-vaccination geometric mean titer antibody responses against four HPV genotypes in HIV-positive and HIV-negative women

GMT antibody against	ATN trial,1 ages 16 to 23 (mean mMu/mL)		ACTG A5240,2 ages 13 to 45 (mean mMu/mL)		HIV-negative controls
	No ART	On ART	CD4 >350	CD4 200-350	
HPV-6	547	1,139	425	327	582
HPV-11	655	1,454	461	388	697
HPV-16	2,176	5,037	1,120	1,077	3,892
HPV-18	445	963	164	166	801

ACTG, AIDS Clinical Trials Group; ATN, Adolescent Trials Network; GMT, geometric mean titer.

Prior research in the general population found that the quadrivalent vaccine protects against most cervical cancers in women, and against cancers of the anus, vagina and vulva.[4] These first two studies in HIV-positive women[1,2] do not prove that the vaccine protects women with HIV from these cancers, only that the vaccine is active against four high-risk HPV types. But since the vaccine is recommended by the CDC for all young women (and for all young HIV-positive men and men who have sex with men),[4] the new findings strengthen that recommendation and show that the vaccine is generally safe in HIV-positive women.

CLINICAL OUTCOME PLUSES IN STARTING ART WITH MORE CD4S: HPTN 052

In HPTN 052, the first trial that randomised HIV-positive people to start ART above 350 or below 250 CD4 cells/mm^3, earlier ART significantly lowered new diagnoses (incidence) of AIDS diseases and tuberculosis.[5] People starting ART immediately – at a CD4 count between 350 and 550 cells/mm^3 – also had a lower rate of all targeted new diagnoses assessed in this updated analysis.

HPTN 052 randomised adults on four continents to begin ART immediately (at a CD4 count between 350 and 550 cells/mm^3) or to wait until their count fell below 250 cells/mm^3 or they had an AIDS disease.[6] The group that started ART immediately had a 96% lower risk of HIV transmission to their HIV-negative steady partner.

The new analysis focused on incidence of AIDS and non-AIDS diseases in the immediate-treatment group versus the delayed-treatment group. The list of primary clinical endpoints included death, World Health Organization (WHO) stage 4 HIV disease, tuberculosis, severe bacterial infection, serious cardiovascular disease, serious liver disease, end-stage renal disease, non-AIDS malignancy and diabetes mellitus. Secondary events were WHO stage 2 or 3 disease, malaria, renal insufficiency, hepatic transaminitis, lipodystrophy, dyslipidemia, hypertension, peripheral neuropathy, lactic acidosis and thrombocytopenia.

The 1,761 HIV-positive participants were monitored for a median of 2.1 years. The immediate group began ART at a median CD4 count of 442 cells/mm^3, compared with 229 cells/mm^3 in the delayed group. HPTN 052 investigators counted 134 people with at least one primary clinical event, including 26 deaths and 21 non-AIDS-related diseases.

There was a strong trend toward shorter time to a first primary event in the delayed-treatment group (P=0.07), and the delayed group had a significantly shorter time to an AIDS disease (P=0.03) or TB (P=0.02). TB incidence was significantly higher with delayed versus immediate treatment (1.8 versus 0.8 per 100 person-years, P=0.009), as was incidence of all primary or secondary clinical events (29.0 versus 24.7 per 100 person-years, P=0.02).

Incidence of a primary event was higher in the delayed-treatment group, but the difference from the immediate group fell short of statistical significance (91 versus 71 per 100 person-years, P = 0.18). Secondary event incidence was significantly greater in the delayed-treatment arm (494 versus 427 per 100 person-years, P=0.05). Statistical analysis that considered time-updated CD4 counts determined that every 50-cell/mm^3 higher count lowered the risk of a primary event 10% (P<0.001). Four other variables were independently associated with primary event risk (Figure 1).

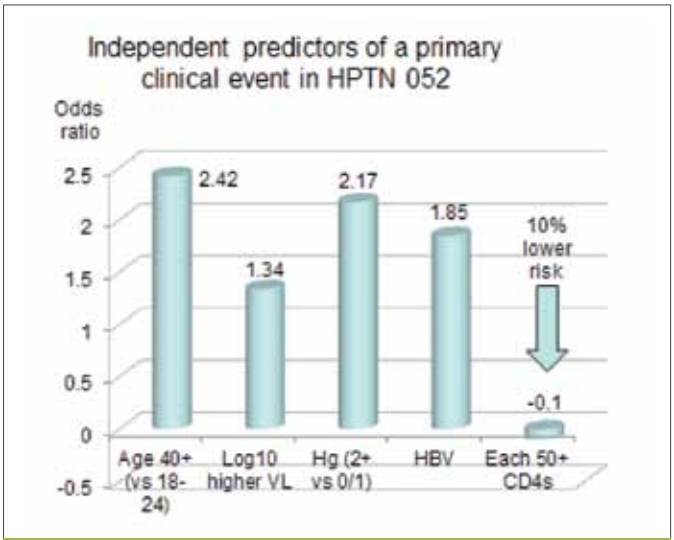

Figure 1. Multivariate analysis identified five factors independently associated with risk of a primary clinical event in HPTN 052.[5] VL, viral load; Hg, hemoglobin grade 2+ versus 0/1; HBV, hepatitis B virus co-infection; CD4s, time-updated CD4 count.

Rates of new non-AIDS diseases were low in both study arms (0.6 and 0.4 per 100 person-years in the delayed and immediate groups).

These clinical results,[5] coupled with the robust preventive effect of earlier ART,[6] should encourage policymakers to reappraise advice on when to start ART. Although the USA and some other countries now recommend starting ART in any HIV-positive person, regardless of CD4 count, WHO and many national guidelines recommend treatment only when the CD4 count falls to 350 cells/mm^3 or lower. The new HPTN 052 results demonstrate a marked clinical advantage to beginning ART at a count above 350 cells/mm^3. In many countries, availability of ample antiretrovirals remains an obstacle to wider access. At AIDS 2012, HPTN 052 investigators proposed that "the combined treatment and prevention benefits of ART support early initiation" of treatment.[5]

NEWER ANTIRETROVIRALS EFFECTIVE IN ART-EXPERIENCED CHILDREN AND TEEN

Three newer antiretrovirals – the integrase inhibitors raltegravir and dolutegravir and the nonnucleoside etravirine – had good antiviral activity in three studies of children and adolescents taking failing regimens.[7-9]

Throughout the world, first-and second-line ART is failing in growing numbers of youngsters. Newer antiretrovirals with activity against resistant HIV are available but had not been widely studied in children and adolescents until these trials.

USA regulators licensed raltegravir for 2- to 18-year-old youngsters after reviewing preliminary results of IMPAACT P1066, which is testing three formulations of this integrase inhibitor in the USA, South America and southern Africa.[7] At AIDS 2012 researchers presented results on adult-dose tablets in two groups of 6- to 18-year-olds (n = 63) and on chewable tablets in weight-based doses for groups of 2- to under-12-year olds (n = 33). More than three-quarters of these youngsters had taken both a protease inhibitor (PI) and a nonnucleoside, and viral load at entry averaged 20,000 copies/mL.

The overall proportion of participants with a viral load below 50 copies/mL after 48 weeks was 56.7% (Figure 2), and 78.9% had at least a 10-fold drop in viral load or a load below 400 copies/mL. Response rates did not differ greatly in younger versus older age groups taking either raltegravir formulation. For comparison, the 48-week raltegravir response rate in adults with triple-class experience was 62% in the BENCHMRK trials.[10] Only 4 children taking raltegravir in IMPAACT P1066 had serious or grade 3 drug-related clinical adverse events or lab abnormalities.

Dolutegravir is an integrase inhibitor in development for antiretroviral-naive or experienced adults. IMPAACT P1093 aimed to assess dolutegravir levels and response rates in youngsters either taking a failing regimen or off treatment for at least eight weeks.[8] No study participants had integrase inhibitor experience. They added dolutegravir to the failing regimen or they began dolutegravir monotherapy if off treatment when entering the study. Children had pharmacokinetic evaluations five to 10 days after dosing began then added an optimised background regimen or substituted such a regimen for the failing combination.

The seven girls and three boys in the study had a median age of 13.5 years (range 12 to 17) and median ART duration of 12.8 years. Nine children had PI experience, and four had taken a nonnucleoside. Baseline viral load averaged about 25,000 copies/mL. Nine youngsters weighing at least 40 kg took 50 mg of dolutegravir once daily, and the tenth youngster took 35 mg once daily, the dose for children weighing between 30 and 40 kg. Other doses being studied are 25 mg daily for children weighing 20 to 30 kg and 20 mg for children under 20 kg.

All children achieved the target 24-hour area under the curve (mean 46.0 µg*h/mL) and the target 24-hour concentration (mean 0.90 µg/mL). Seven children reached a viral load below 40 copies/mL four weeks after starting dolutegravir plus a background regimen, and nine reached a load below 400 copies/mL. No children stopped dolutegravir because of adverse events, and there were no drug-related adverse events.

Etravirine is a nonnucleoside with activity against some virus resistant to nevirapine and efavirenz. The PIANO trial was an international study of etravirine plus a ritonavir-boosted PI and at least one other active antiretroviral in 41 children six to 12 years old and in 60 adolescents 12 to 18 years old.[9] All children had a viral load above 500 copies/mL and antiretroviral experience; while 44% had taken nevirapine, 40% had taken efavirenz. Study participants took etravirine at a dose of 5.2 mg/kg twice daily to a maximum dose of 200 mg twice daily. Thirty-four children and 42 adolescents (75% overall) completed the trial.

After 48 weeks a noncompletion-equals-failure analysis determined that 68% of children, 48% of adolescents and 56% overall had a viral load below 50 copies/mL. These rates were similar to the 61% response rate in antiretroviral-experienced adults in the DUET trials.[11] (The lower response rate in adolescents than children reflects their greater nonnucleoside experience, more advanced disease and worse adherence. The trial was not powered to rate response differences

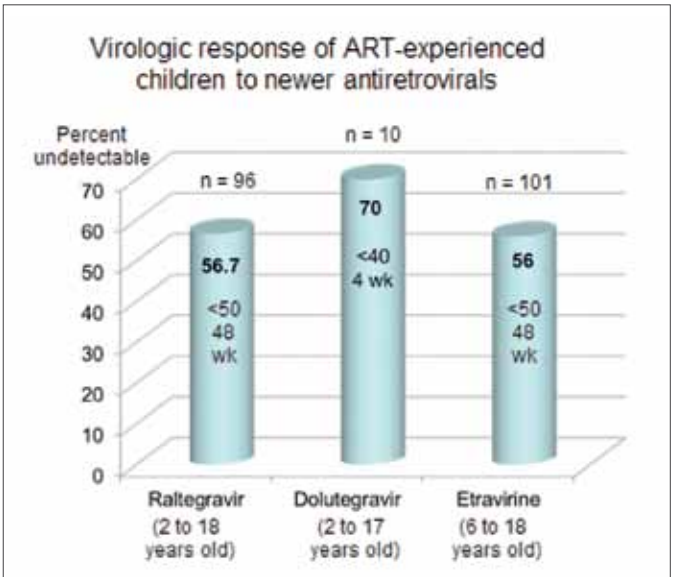

Figure 2. Antiretroviral-experienced children and adolescents in three trials attained good response rates to rescue regimens containing raltegravir, dolutegravir or etravirine.[7-9] The raltegravir response rate compared with a rate of 62% in adults in the BENCHMRK trials,[10] and the etravirine response rate compared with a rate of 61% in adults in the DUET trials.[11]

AIDS 2012 volunteer.
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between children and adolescents.) Among 30 youngsters with genotypic data after failure, 18 (60%) had nonnucleoside-related mutations. Rates of adverse events leading to discontinuation were 5% among children and 10% among adolescents.

Across the world approximately 3.4 million children under 15 were living with HIV in 2011, and only 562,000 of them (16.5%) were receiving ART, a treatment rate much lower than in adults.12 Two reasons for relatively low antiretroviral coverage in children are lack of formulations appropriate for children and lack of research on antiretroviral pharmacokinetics, efficacy and safety. These problems are especially acute after failure of first- or second-line regimens in children, because third-line regimens are not available in many high-prevalence areas. These studies demonstrate that third-line regimens can be effective in children and adolescents, but the problem of availability remains.

GOOD RESULTS WITH NEW ANTIRETROVIRALS IN ART-NAIVE OR EXPERIENCED ADULTS

Several randomised trials reported at AIDS 2012 showed that new agents to treat HIV infection are statistically non-inferior to older agents in adults with chronic HIV infection.

After 96 weeks of treatment in a 712-person trial, the investigational integrase inhibitor elvitegravir was noninferior to the licensed integrase inhibitor raltegravir (each with a ritonavir-boosted PI and one other agent) in antiretroviral-experienced adults.[13] Patients randomised to elvitegravir in this double-blind, active-controlled trial had a lower rate of liver enzyme elevations than did those randomised to raltegravir, but otherwise adverse event rates were similar in the two treatment arms.

Elvitegravir is being co-formulated with cobicistat, a boosting agent without antiviral properties that can also boost PIs. A 692-person, double-blind, double-dummy trial randomised antiretroviral-naive adults to cobicistat or ritonavir to boost the PI atazanavir (plus tenofovir/emtricitabine).[14] After 48 weeks the cobicistat regimen proved virologically noninferior to the ritonavir regimen, and adverse event rates were similar in the two arms.

Dolutegravir, another investigational integrase inhibitor, proved noninferior to raltegravir after 48 weeks in a double-blind, placebo-controlled phase 3 trial that randomised 822 antiretroviral-naive adults to one of these agents plus two nucleosides.[15] Rates of adverse events that affected at least 5% of participants did not differ between the two study arms.

A randomized, open-label, 476-person trial that enrolled adults with a viral load below 50 copies/mL while taking a ritonavir-boosted PI regimen found that switching to co-formulated rilpivirine (a nonnucleoside) plus tenofovir/emtricitabine maintained virologic control through 24 weeks.[16] Lipid profiles improved significantly in patients who switched to rilpivirine.

RESISTANCE RATES AND RISKS IN PATIENTS INFECTED WITH SUBTYPE C HIV-1

Two large studies explored rates of treatment-acquired resistance to antiretrovirals in South Africans, most of whom are infected with HIV-1 subtype C.

Genotyping of 240 adults who began first-line ART at 17 clinics in rural Hlabisa determined that 208 (87%) had at least one resistance mutation after a median 42 months of treatment.[17] The high resistance rate reflects the extended time patients took a failing antiretroviral regimen, a median of 27 months. More than four in five patients (81%) had a mutation conferring resistance to nonnucleosides. Genotypic sensitivity scores indicated that detected mutations significantly compromised standard second-line antiretroviral options in 40 patients (17%). The investigators believe their results suggest "a role for genotypic resistance-testing in routine care" in settings like this.

Genotypic analysis of 1,525 viral specimens from 1,293 children and adults treated across South Africa from 2006 to 2011 recorded a steady increase in tenofovir or abacavir use, with declines in use of stavudine, zidovudine, and didanosine.[18] The tenofovir-related K65R mutation emerged in 2 of 28 patients (7%) taking tenofovir with lopinavir/ritonavir, 33 of 105 (31%) taking tenofovir with efavirenz, and 7 of 8 (88%) taking tenofovir with nevirapine ($P = 0.009$ for efavirenz versus nevirapine). The L74V mutation emerged in 4 of 71 patients (6%) taking abacavir with lopinavir/ritonavir, 22 of 50 (44%) taking abacavir with efavirenz, and 2 of 4 (50%) taking abacavir with nevirapine. The researchers proposed that lopinavir/ritonavir protects against emergence of tenofovir- or abacavir-associated resistance mutations. They noted that overall prevalence of tenofovir-associated mutations is high, a finding reflecting results of another study of subtype C-infected South Africans.[19]

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TRACK C: EPIDEMIOLOGY AND PREVENTION SCIENCE

TREATMENT AS PREVENTION AND TEST – AND -TREAT STRATEGIES

HPTN 052, a four-continent randomised trial, established the principle that treating HIV-positive people at a higher CD4 count lowers the risk that they will transmit the virus to steady sex partners.[1] This study recruited 1,763 HIV-discordant couples whose HIV-positive partner had a CD4 count between 350 and 550 cells/mm^3 and randomised those partners to immediate antiretroviral therapy (ART) or to wait until they had a CD4 count below 250 cells/mm^3 or an AIDS disease. Immediate treatment cut the risk of HIV transmission to the Several reports at AIDS 2012 offered further analysis of HPTN 052 and of related studies of the test-and-treat strategy, which calls for expanded HIV testing and immediate treatment of everyone who tests positive. Some of this research raised questions about how effective test-and-treat will be in practice rather than in a carefully controlled trial.

A systematic review of observational studies confirmed a lower risk of HIV transmission when an HIV-positive partner is taking ART.[2] This analysis focused on seven studies that recorded 436 HIV transmissions, 71 (16%) in couples with an antiretroviral-treated positive partner and 365 (84%) in couples with an untreated positive partner. Multivariate analysis determined that ART lowered the transmission rate 66% (rate ratio [RR] 0.34, 95% confidence interval [CI] 0.13 to 0.92). After elimination of two studies with inadequate person-time data, ART cut the transmission rate 84% (RR 0.16, 95% CI 0.07 to 0.35). When the researchers limited the analysis to HIV-positive partners with a CD4 count above 350 cells/mm^3, as in HPTN 052, ART cut the transmission rate 98% (RR 0.02, 95% CI 0.00 to 2.87). In this final analysis, all 61 HIV transmissions occurred in couples with untreated positive partners.

A modelling study using data from HPTN 052 couples in South Africa and India determined that starting ART at a CD4 count above 350 cells/mm^3 would prolong survival, be cost-effective, and prevent HIV transmission.[3] But the transmission benefit held true only over the short term.

Anthony S. Fauci, Director of the National Institute of Allergy and Infectious Disease at the National Institutes of Health (NIH) speaks at AIDS 2012.
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The investigators defined "cost-effective" as less than three times per capita gross domestic product (GDP) and "very cost-effective" as less than one times GDP. South Africa has a per capita GDP of US$8,100, while India has a per capita GDP of $1,400.

In South Africa immediate ART (>350 cells/mm^3) would increase survival, prevent early transmissions, and prevent costly opportunistic infections, which partly offset the cost of ART. Immediate antiretroviral treatment in South Africa would be very cost-effective through 5 years of treatment ($700 per year of life saved [YLS]) and over a lifetime ($1,200/YLS). In India early ART would prevent opportunistic infections, but the money saved would not offset antiretroviral costs as much as in South Africa, because in India ART is expensive relative to treating other diseases. Early ART would be cost-effective through 5 years in India ($2,900/YLS) and would become very cost-effective over a lifetime ($1,300/YLS).

Compared with delayed ART, immediate ART would cut HIV transmissions through the first 5 years of treatment in both South Africa and India. In South Africa immediate ART compared with delayed ART would lower transmissions 59% through 5 years; in India early ART would lower transmissions 57% through 5 years. But the impact of immediate ART on transmissions disappeared over a lifetime because chances of transmission increase with longer life.

Françoise Barré-Sinoussi, IAS President, at the Towards an HIV Cure press conference.
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The researchers cautioned that their findings pertain specifically to HPTN 052 trial participants and may not apply to people not in trials or not in steady partnerships.

When people use an effective HIV prevention strategy (like ART, pre-exposure prophylaxis or circumcision), they may be tempted to abandon safer-sex practices (like regular condom use). But that did not happen in HIV-discordant couples enrolled in HPTN 052.[4] Risky-sex rates were low in trial participants when the study began: only 4.0% in the immediate-treatment group and 5.7% in the delayed-treatment group reported condom-free vaginal sex with a primary partner. Three months after these people entered the trial, the rate of unprotected vaginal sex fell to 2.9% in the immediate group and to 3.0% in the delayed group. Rates of unprotected sex continued to decline through 2 years of follow-up, with no substantial difference between study arms. The rate of unprotected anal intercourse was low when HPTN 052 began (<0.3%) and throughout follow-up. Rates of unprotected sex in HPTN 052 participants may not reflect what happens among people not enrolled in a trial, since trial participants typically have more frequent follow-up and more diligent risk-reduction counselling.

A study in rural Uganda showed that a test-and-treat approach to HIV care does not necessarily lower sexual transmission of the virus in discordant couples, perhaps especially in a setting where viral load monitoring is not routine.[5] This study involved 586 stable, cohabitating, discordant couples with 348 HIV-positive partners (59%) on ART or starting ART (because of a CD4 count <250 cells/mm^3) and 238 positive partners not on ART. All HIV-negative study participants got tested for HIV every 3 months, and everyone received risk-reduction counselling, condoms and medical care, but that care did not include routine viral load monitoring of positive partners.

Couples with an antiretroviral-treated partner were more likely to report condom use at last sex (67% versus 58%, P=0.001) and longer relationships (12 versus 10 years, P=0.018). But couples with a treated positive partner had a lower circumcision rate (P=0.053). The new HIV infection rate was 2.09 per 100 person-years in the ART group and 2.30 in the untreated group, and that difference lacked statistical significance (incidence rate ratio 0.91 in treated participants, P=0.84). Only 7% of all antiretroviral-treated people had a viral load above 1,000 copies/mL, but they accounted for three of the nine transmissions in the ART group. Cox proportional hazards modelling determined that ART did not lower the risk of HIV transmission, even after statistical adjustment for circumcision or HSV-2 infection of negative partners.

This nonrandomised observational study cannot be compared directly with HPTN 052[1] for several reasons.

(1) Lack of viral load monitoring resulted in inability to detect at least nine people in whom treatment failed with a viral load above 1,000 copies/mL, raising their chance of transmitting HIV. (Viral load monitoring occurred every 6 months in HPTN 052.)

(2) No one in this cohort began treatment until their CD4 count fell below 250 cells/mm^3, which was the start point for the delayed-treatment group in HPTN 052.

(3) The researchers were unable to determine genetically whether the positive person in the couple, or someone outside the couple, infected the negative partner. (Transmissions were genetically confirmed in HPTN 052.) Still, this enlightening study from a country where HIV rates may be rebounding indicates that treatment (starting at a CD4 count below 250 cells/mm^3) does not necessarily lower HIV transmission risk in a high-prevalence community.

Research in the USA underlined another reason why treatment-as-prevention may not work in some communities: irregular condom use by treated people with a detectable viral load.[6] This 5,411-person five-city study focused on adults in routine HIV care who underwent testing for antiretroviral adherence, substance use, HIV risk behaviour and other variables. Researchers defined being at risk for transmitting HIV as current sexual activity with a detectable viral load and with incomplete or no condom use in the prior 6 months.

The investigators found that 1,200 people (22%) used condoms inconsistently with an undetectable viral load and 356 (7%) used condoms inconsistently with a detectable

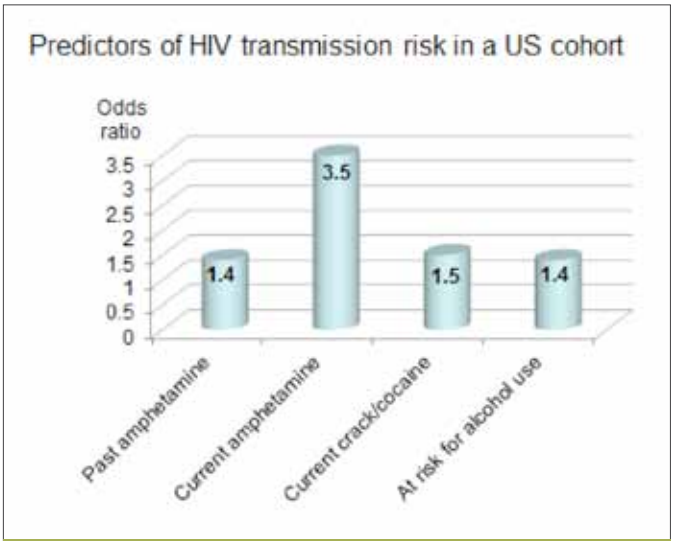

Figure 1. Four substance-related factors independently predicted being at risk for HIV transmission in a cohort of USA patients in care for HIV infection.[6]

viral load. Statistical analysis adjusted for age, race, study site and depression score identified four substance use habits that independently raised the odds of being at risk for HIV transmission: past amphetamine use, current amphetamine use, current crack/cocaine use and being at-risk for alcohol use (Figure 1). A significantly higher proportion of people at risk for transmission had 2 or more sex partners in the past 6 months (54% versus 19% not at risk, P<0.001).

Despite these cautionary findings from low- and high-income countries, a modelling study determined that elimination of HIV with a test-and-treat strategy may be in reach in some countries, but perhaps not in certain high-prevalence countries, like South Africa.[7] Dutch researchers extended the HIV elimination model developed by Granich and colleagues[8] to incorporate more accurate assumptions of HIV disease progression (from CASCADE cohort data) and variable infectivity. The model determines an elimination threshold as a function of testing coverage and adherence to ART.

This type of analysis hinges on the variable R_0, the number of secondary HIV infections resulting from one primary infection in a susceptible population. The Dutch team figured that HIV elimination is not possible if R_0 is greater than 6. Population data indicated that R_0 is greater than 6 in South Africa, as well as in England and Wales. But R_0 is below 6 in France and Germany and among men who have sex with men (MSM) in the Netherlands. The investigators concluded that "elimination is only feasible for populations with low basic reproduction numbers [R_0] or if the reproduction number is lowered significantly as a result of other additional interventions." They stressed that high infectivity during primary HIV infection significantly raises the elimination threshold.

Together, results of these studies suggest that more intense screening for HIV infection and prompter treatment of positive people will not automatically lower HIV transmissions and incidence. In 2009, a modelling study by WHO researchers determined that "universal voluntary HIV testing and immediate ART, combined with present prevention approaches" could cut HIV incidence and mortality to less than one per 1,000 people within 10 years of a implementing this strategy.[8] Other modelling experts, including Dutch researchers who described a new model at AIDS 2012,[7] argue that the assumptions in the WHO model are overly optimistic.

Findings in contemporary cohorts of HIV-positive people in care illustrate key obstacles to success with the test-and-treat approach (Figure 2). USA researchers found that 29% of adults in care for HIV do not use condoms consistently, and 7% do not use condoms consistently and have a detectable viral load.[6] A systematic review of seven observational studies involving HIV-discordant couples confirmed the HPTN 052 finding of lower transmission risk in couples with a treated positive partner.[2] But a large cohort study in rural Uganda, where viral load monitoring for HIV-positive people is not routine, found similar HIV transmission rates in HIV-discordant couples with an antiretroviral-treated positive partner and in couples with an untreated HIV-positive partner.[5] These researchers cautioned that "it is difficult to extrapolate the results of randomised controlled trials [like HPTN 052] in ideal situations to real life setting[s] in low-income countries." They proposed that their results "do not question that ART works as a prevention tool, only that the effect can be undermined by other biological, social and cultural factors which also affect HIV transmission risk."[5]

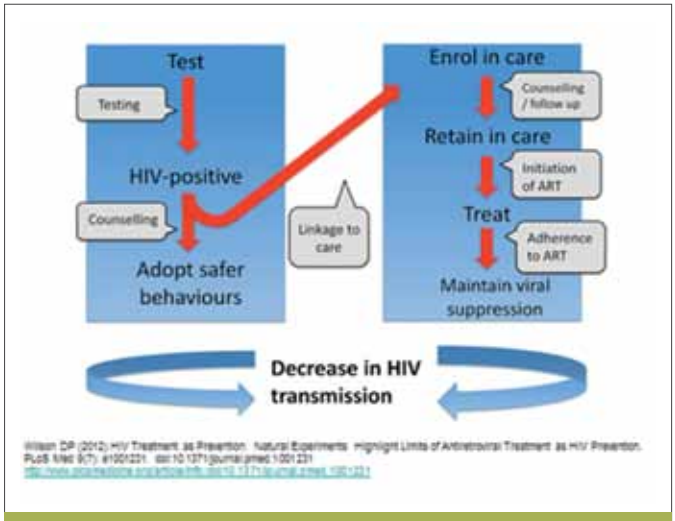

Figure 2. Antiretroviral therapy to prevent HIV transmission will work at the population level only if high proportions of people get tested, adopt safer behaviours, enroll in care if positive, remain in care and reach and maintain an undetectable viral load.

Diagram: From Wilson DP.9

Speaking at an HIV paediatrics workshop immediately before AIDS 2012, HPTN 052 principal investigator Myron Cohen voiced his belief that viral load monitoring is essential to make a test-and-treat strategy work. He called for continuing work to develop simple, inexpensive viral load assays for use in low-income settings. Cohen also noted a review of "natural experiments in treatment as prevention" by David Wilson which showed that wide HIV testing and treatment of MSM in Australia has not limited new HIV diagnoses there.[9]

Two other often-cited "natural experiments" in treatment as prevention involve HIV communities in British Columbia, Canada,[10] and San Francisco.[11] In both places, increasing rates of HIV testing, treatment and viral suppression have been linked to falling HIV diagnosis rates, findings suggesting that wider testing and treating stymies HIV transmission. But Wilson observes that in San Francisco the rate of new HIV infections is still relatively high, and in British Columbia "declines in [HIV] incidence could be attributed to other prevention programmes specifically targeting this population group over the same period."[9]

AIDS 2012 poster exhibition area.
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A June 2012 WHO programmatic update sought to find a balance between immediate treatment needs in low- and middle-income countries and treatment as prevention (TasP).[12] "It is certain that TasP needs to be considered as a key element of combination HIV prevention and as a major part of the solution to ending the HIV epidemic," the update states. "In the short and medium term, while countries are concentrating their efforts on scaling up treatment according to the eligibility criteria recommended by WHO, it is expected that they will concurrently identify opportunities to maximise the use of ART for prevention purposes (TasP)."[12]

Around the time of AIDS 2012, PLoS Medicine published nine TasP analyses, available at http://www.plosmedicine.org/article/browseIssue.action?issue=info:doi/10.1371/issue.pmed.v09.i07.

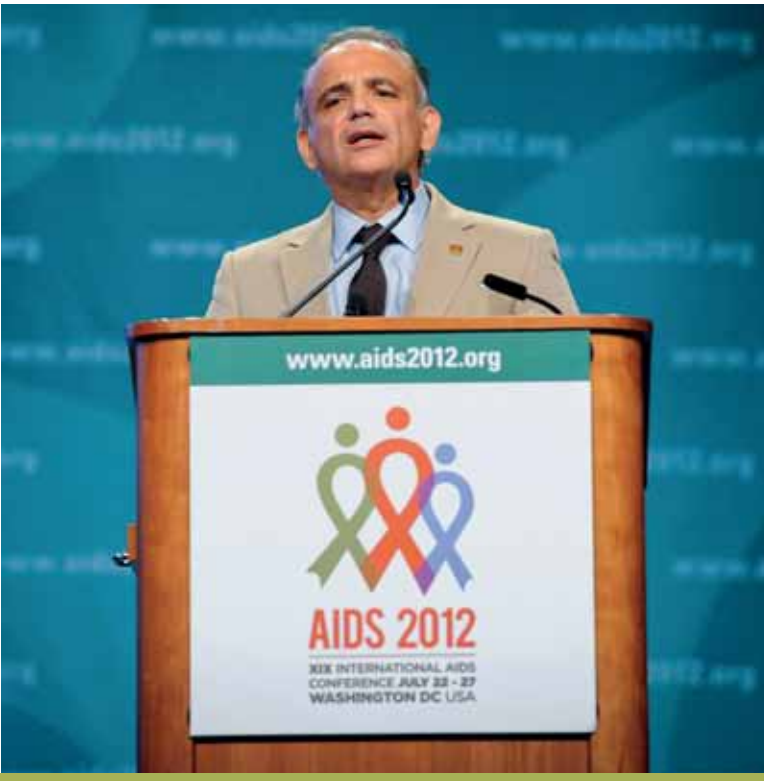
PrEP FOR HIGH-RISK COUPLES, AND NEW PrEP CANDIDATES

Daily tenofovir/emtricitabine (TDF/FTC) was licensed for pre-exposure prophylaxis (PrEP) in the USA after three placebo-controlled trials found that this antiretroviral combination lowers HIV acquisition risk in at-risk heterosexual couples,[13] men and women,[14] and MSM.[15] But TDF/FTC PrEP or TDF PrEP did not protect high-risk African women from HIV in two other placebo-controlled trials,[16,17] findings leading some to propose that PrEP with these drugs will not work in people with the highest HIV risk. To address that hypothesis, Partners PrEP investigators[13] assessed the efficacy of TDF PrEP and TDF/FTC PrEP in HIV-negative partners in the highest-risk HIV-discordant couples they studied in Kenya and Uganda.[18]

The researchers identified couples with a high HIV transmission risk by using a risk score that included age of the negative partner, number of children, circumcision status, marriage/cohabitation status, unprotected sex with a partner in the prior 30 days and viral load of the positive partner. Of the 4,758 couples originally assessed, there were 346 high-risk couples in the TDF PrEP arm, 354 in the TDF/FTC PrEP arm and 380 in the placebo arm. HIV incidence was 1.34 per 100 person-years in the TDF arm, 1.10 in the TDF/FTC arm and 5.01 in the placebo arm. Those findings meant TDF PrEP lowered the risk of HIV acquisition 72% in high-risk couples (P=0.001 versus placebo), while TDF/FTC PrEP cut the risk 78% (P<0.001 versus placebo).

Partners PrEP investigators argued that "our data do not support the hypothesis that the futility of PrEP in [FEM-PrEP and VOICE] was a result of higher HIV-1 transmission risk."[18]

TDF/FTC is the first well-tested PrEP agent, but it will not be the last. At AIDS 2012, for example, researchers presented results of a phase 1 dose-escalation study of a parenterally administered integrase inhibitor, S/GSK1265744, in healthy adults.[19] The experimental agent is suspended in nanoparticles that gradually degrade and release an active drug that maintains high levels in plasma.



Luiz Loures from UNAIDS speaks at an AIDS 2012 session.
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The study involved 56 healthy HIV-negative volunteers randomised to receive placebo or S/GSK1265744 in intramuscular or subcutaneous doses of 100, 200, 400 or 800 mg. The injected integrase inhibitor achieved plasma half-lives of 21 to 50 days, compared with 30 to 40 hours in a study of orally administered S/GSK1265744. At an intramuscular dose of 80 mg, S/GSK1265744 attained a day-10 concentration 21-fold above the protein binding-adjusted 90% inhibitory concentration and comparable to exposure seen with 30-mg once-daily oral dosing. In an earlier study, that oral dose yielded a 2.5 log10 decrease in viral load after 10 days of monotherapy. Most study participants reported mild injection-site reactions.

S/GSK1265744 is being evaluated as PrEP as well as for treatment of HIV infection in combination with long-acting rilpivirine, a nonnucleoside. Previous research showed that a single 600-mg intramuscular dose of rilpivirine remained in the circulation for 84 days in 10 women and 6 men without HIV.[20]

Although the FDA licensed daily TDF/FTC for PrEP in the USA, much remains to be learned about this approach to preventing HIV acquisition. Discussing disparate results of PrEP and microbicide trials, Myron Cohen and Lindsey Baden called for additional research "to allow a proper understanding of the potential efficacy of and adverse events associated with pre-exposure prophylaxis and to identify other factors that might influence efficacy."[21]

Among still-unanswered questions are the long-term side effects of TDF/FTC in healthy HIV-negative people and whether HIV testing and follow-up retesting of PrEP users will be sufficient to prevent newly infected people from exposing themselves to development of resistant HIV. Whether HIV-negative people will take TDF/FTC PrEP daily, as recommended, also remains unknown. TDF/FTC adherence varied substantially in clinical trials, despite ongoing counselling. PrEP users must also be counselled not to abandon other safer-sex practices, including regular condom use. Finally, the affordability of PrEP for people at high risk for HIV infection remains to be determined.

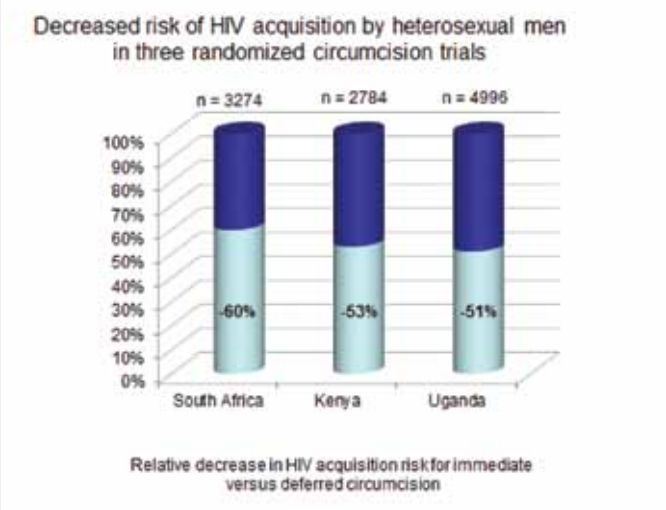

Figure 3. In three randomized trials,[22-24] circumcision of heterosexual men lowered the risk of HIV acquisition by approximately 50% to 60%.

A comprehensive review of PrEP data and analysis of implications for primary care use are online at http://www.clinicaloptions.com/HIV/Treatment%20Updates/PrEP%20in%20Primary%20Care/CCO%20Slideset/PrEP_Primary_Care_Slides.aspx.

SIMPLER CIRCUMCISION METHODS HOLD PROMISE OF WIDER USE

Three randomised trials demonstrated that medical male circumcision lowers the risk of HIV acquisition in heterosexual African men by about 60% (Figure 3).[22-24] Although WHO endorses circumcision as an element of HIV prevention in eastern and southern Africa[25] and some high HIV-prevalence countries are increasing capacity to perform circumcisions, the operation requires trained surgical staff and commitment of operating-room time. AIDS 2012 offered results of research on two simple circumcision methods that require less expertise and time.

AIDS 2012 Friday Plenary Press Conference - Anthony Harris, International Union Against Tuberculosis and Lung Diseases, France
Photo: © IAS/Deborah W. Campos - Commercialimage.net

With the Shang Ring procedure, foreskin is everted over an inner ring, an outer ring is applied, and foreskin is excised from the underside (Figure 3).[26] Shang Ring surgery is minimally invasive and does not require hemostasis or suturing, but the rings must stay in place for seven days. This trial randomised 400 men to conventional circumcision surgery (forceps-guided in Kenya or dorsal-slit in Zambia) or to the Shang Ring procedure.

One hour and 2 days after the procedures, pain rated on a visual analogue scale was similar with the Shang Ring and with conventional surgery. Wound healing occurred an average of 5.2 days earlier with the Shang Ring than with surgery (P<0.0001). There were no severe adverse events with either type of circumcision, and total adverse events rates were similar with the Shang Ring (3.6%) and surgery (3.5%).

Patient-reported post-procedure appearance satisfaction rates with the Shang Ring versus surgery were 95.7% versus 85.9% in Kenya (P<0.02) and 96.8% versus 71.3% in Zambia (P<0.0001). Average time to complete the Shang Ring procedure was 7.0 minutes in Kenya and 7.3 minutes in Zambia versus 20.7 and 19.8 minutes for surgery (P<0.0001 for both comparisons). Among six providers (four non-physicians and two physicians), five rated the Shang Ring "much easier" than surgery and one rated the Shang Ring "easier."

The PrePex procedure places an inner elastic ring around the foreskin, guided by two plastic rings. The procedure is bloodless and does not require a sterile setting, injected anesthesia or sutures (Figure 4). This study involved 10 nurses with no circumcision experience who received three days of training and formed five teams.[27] They circumcised 590 men with PrePex, and follow-up lasted eight weeks.

There were five adverse events (0.85%), all moderate in severity, two (0.34%) related to the device, one (0.17%) related to the procedure and two (0.34%) related to neither. All problems were resolved during follow-up. All 590 men achieved complete circumcision with the glans fully exposed. Complete healing occurred an average of 33 days after device removal. Total time to prepare for and complete the procedure decreased by an average four minutes and 39 seconds from the first 125 men circumcised to the last 125.

Rwanda received WHO endorsement to scale up PrePex circumcision after visiting and auditing studies.[28] The country has conducted more than 4,200 PrePex circumcisions to date. Rwanda plans a pilot study of 10,000 PrePex circumcisions to inform scale-up and aims to complete 2 million circumcisions in 2 years with 150 teams of 2 nurses working full-time on circumcision. They hope to complete 54 procedures per team per day.

Together these studies offer evidence that circumcision can be completed safely and effectively after brief training of non-physician professionals. These simpler circumcision procedures could help lower HIV incidence in high-prevalence countries with a shortage of trained physician surgeons. WHO notes that 10% to 15% of adult Rwandan men were not eligible for PrePex circumcision because of phimosis or narrow opening of the foreskin.[28] The WHO report stresses that "appropriate counselling on sexual abstinence and condom use after male circumcision and before complete healing is always crucial, but it is particularly crucial with use of [PrePex] because the healing time is at least one week longer than with standard surgery."[28]

RISK OF HIV ACQUISITION WITH HORMONAL CONTRACEPTION

Further analysis of a large African cohort confirmed that injected hormonal contraceptives double the risk of HIV acquisition by African women,[29] but a systematic review concluded that definitive evidence is still lacking on HIV acquisition risk with injected hormonal agents.[30]

Earlier in 2012, Partners in Prevention researchers in east and southern Africa published a prospective study of 3,790 HIV-discordant couples in whom hormonal contraceptive use doubled the risk of HIV acquisition by women and doubled the risk of HIV transmission from women to men.[31] HIV risk was highest with injected hormonal contraceptives. But studies in other cohorts have not consistently confirmed these associations. After considering research on this question, WHO maintained its advice not to restrict use of hormonal contraceptives to avoid unintended pregnancies.[32] Women using progestogen-only injectable contraceptives, WHO advised, should also use condoms or other measures to prevent HIV infection.

At AIDS 2012, Partners in Prevention researchers[31] reported results of additional Cox proportional hazards sensitivity analyses to test the strength of their original finding. In every sensitivity analysis, hormonal contraceptive use at least doubled the risk of HIV acquisition by women with a positive partner.[29] A statistical model adjusted for number of sex acts confirmed a doubled risk of HIV infection with injectable contraceptive use versus no hormonal contraceptives (adjusted hazard ratio [aHR] 2.06, 95% CI 1.04 to 4.07, P=0.04). In a model adjusted for the male partner's report of sex without a condom, the woman's HIV risk with injectable contraceptives remained doubled (aHR 2.03, 95% CI 0.95 to 4.32, P=0.07).

When the researchers limited the analysis to a subgroup of women who reported unprotected sex, HIV risk with injectable hormones was more than doubled (aHR 2.29, 95% CI 0.70 to 7.53, P=0.17), as it was during periods that included only visits before a first switch in contraceptive methods (aHR 2.62, 95% CI 0.93 to 7.33, P=0.07). A final analysis focused only on presumed consistent DMPA users and thus eliminated women from South Africa. In this model, injectable contraception more than tripled chances of HIV infection when compared with use of no hormonal contraception (aHR 3.39, 95% CI 1.38 to 11.22, P=0.01).

The researchers noted that some associations had P values greater than 0.05 because of reduced statistical power in these analyses, "but the magnitude of association continued to be as strong as that seen in our primary analytic model."[29]

A systematic review of research on hormonal contraception and HIV acquisition in women included randomised trials or cohort studies published through 15 December 2011.[30]

All studies compared HIV-negative women using hormonal contraception with HIV-negative women not using hormonal agents. The analysis included seven studies of oral contraceptive pills, three studies of norethisterone enantate and eight studies of injectable hormonal contraceptives. The researchers concluded that available data do not suggest an association between oral contraceptives or norethisterone enantate and HIV acquisition. For the injectable hormonal DMPA, they concluded that available data "neither establish a clear causal association nor definitely rule out the possibility of an effect on risk of HIV acquisition."[30] (A separate systematic review concluded that "the preponderance of evidence… indicates that use of oral contraceptives or of DMPA does not affect HIV disease progression among women with HIV.[33])

Understanding the impact of injectable hormonal contraceptives on HIV risk is critical because reliable contraception is essential to family planning, and many women favour injectable hormonal contraception because of its convenience and durability. Assessing the import of their study in east and southern Africa, Partners in Prevention researchers stressed that "the benefits of injectable contraceptives are unequivocal and must be balanced with the potential risk for HIV-1 infection."[29] They emphasised the need to integrate reproductive health care and HIV prevention programmes, and they called for more high-quality studies of hormonal contraceptives and HIV risk.

"Because of the inconclusive nature of the body of evidence on possible increased risk of HIV acquisition" with injected hormonal contraceptives, WHO counsels, *"women using progestogen-only injectable contraception should be strongly advised to also always use condoms, male or female, and other HIV preventive measures"*[32].

AIDS 2012 Friday Plenary Press Conference, Judith Currier, University of California, Los Angeles, and Yogan Pillay, National Department of Health, South Africa.
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AIDS 2012 Opening Session – Arash and Kamiar Alaei receive the IAS/amfAR award by Sharon Stone, amfAR Global Fundraising Chairman.

TRACK D: SOCIAL SCIENCE, HUMAN RIGHTS AND POLITICAL SCIENCE

MARGINALIZED POPULATIONS AT HIGHER RISK FOR HIV

Findings that the HIV epidemic in sub-Saharan Africa countries concentrates in people of higher socioeconomic status are often disputed. Basing his conclusions on two successive USAID national surveys in each of four African countries, James Hargreaves (London School of Hygiene and Tropical Medicine) showed that HIV is initially more prevalent in higher socioeconomic strata[1]. As the epidemic evolves, poorer sectors of the population eventually are afflicted with higher HIV rates. In the four countries studied (Kenya, Lesotho, Malawi and Tanzania), HIV prevalence generally rose in uneducated populations (except for Lesotho women) while it generally fell in those with a secondary education (except for Malawi women). Hargreaves ascribed this trend to the ability of better-off citizens to make greater use of HIV prevention education.

Heather Worth (University of New South Wales, Sydney, Australia) extended this analysis to look at correlations with antiretroviral therapy (ART) coverage on a national level[2]. Her study found that a higher percentage of ART-eligible patients are receiving ART in countries with higher GDP per capita, higher literacy rates and greater gender equality. The influence of these and other economic measures became statistically insignificant when indicators of governance quality were included in a multivariate analysis. Greater popular political input and stability were important, but the governmental factor with the strongest correlation with ART use was reduced corruption.

Treatment success is of course based on high adherence to dosing schedule, and just having ART available does not mean that patients take it consistently. Craig Phillips (University of Ottawa, Ottawa, Canada) described a survey of treatment adherence among 2,182 persons with HIV living in five national entities (Canada, China, Namibia, Thailand, Puerto Rico and the USA)[3].

This study's findings specifically refuted the hypothesis that inequality in wealth distribution has a direct influence on low treatment adherence among a country's residents. After controlling for location, gender, age, time since HIV diagnosis, and adherence self-efficacy (confidence in one's ability to follow prescription instructions), the researchers found three variables that correlated with improved adherence among a country's residents. These were the country's overall democracy ranking, HIV criminalization and social capital score.

Democracy ranking again relates to governance quality. HIV criminalization – a measure of the likelihood that people with HIV will be prosecuted for acts or omissions related to their disease – is an indicator of the stigma associated with HIV. Social capital measures the strength of the community members' social networks. Although this effect is nuanced[4, 5, 6], enhanced community cohesion generally leads to access to additional health services and improved health[7]. Social networks will be weaker in places where the populations with HIV are more marginalized and HIV itself more stigmatized.

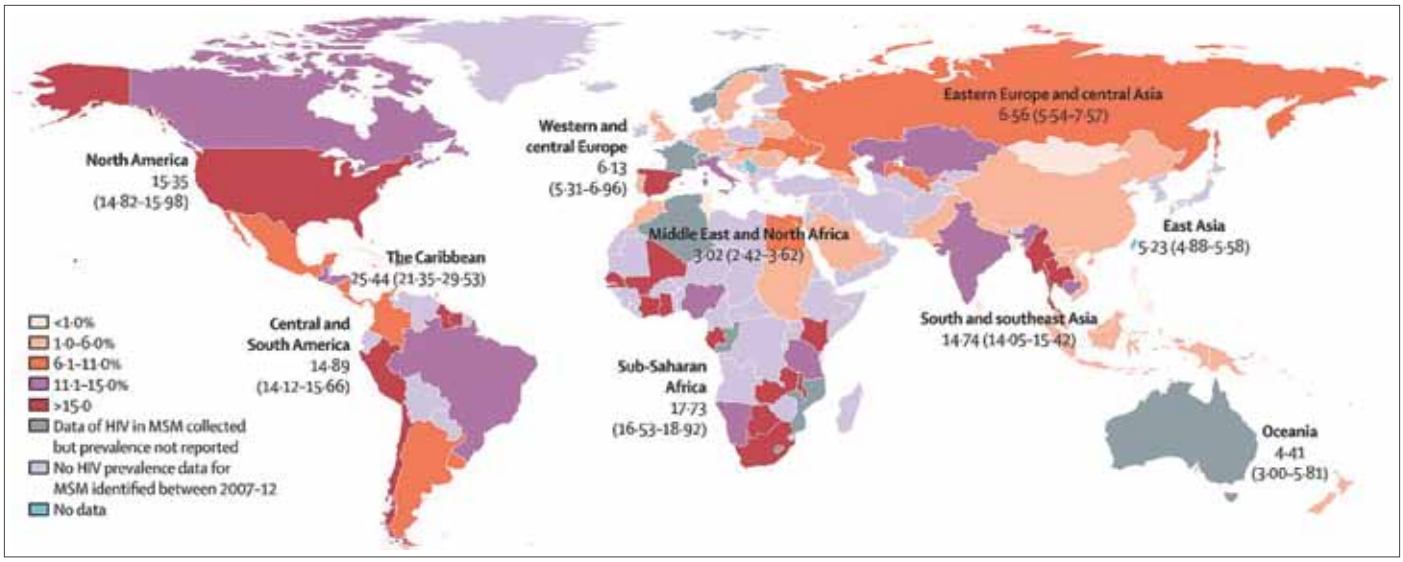
STIGMATIZATION OF MSM ACCELERATES THE EPIDEMIC

Prejudice against men who have sex with men (MSM) is strong around the world, and it most particularly affects young MSM. These men are more dependent on their families than older MSM. They are less experienced than older MSM in countering homophobia. Their reduced life skills in this area partly stem from their limited knowledge of sexual health and legal rights. Glenn-Milo Santos (University of California San Francisco, San Francisco, USA) described a global telephone survey of MSM that highlighted the results of this vulnerability.[8] The 1,428 young MSM (age 30 or below, 14% HIV+, 34% never tested for HIV) were less likely than older MSM to report easy access to HIV prevention services (e.g. easy access to condoms was reported by 36% of young MSM and 47% of older MSM). The same was true of access to ART (33% vs. 59%, respectively). Perceived negative social attitudes to homosexuality were the greatest predictor of young MSMs' self-reported lack of HIV prevention services, and self-reported internalized negative feelings were another a significant restrictive factor here.

A survey in Malawi, an area of high HIV prevalence (11% in the general 15-49 year-old population) looked at the factors promoting HIV acquisition among MSM of all age groups[9]. The survey's 339 respondents, who were recruited via social networks, commonly exhibited fears of disclosure of their sexual practices, with 20% at least once avoiding healthcare for this reason. Only 22.5% reported ever receiving HIV prevention information. HIV prevalence was 14.8%, and 90% of the HIV-positive respondents were unaware of their status until they were tested as part of the survey. Multivariate analysis found that age above 25 years, previous imprisonment and having at least one child were significantly associated with HIV infection. Conversely, rural residency and a secondary or college education were protective.

Another survey – of nearly 2,800 Indian MSM, transgenders and hijras – also found widespread fear of disclosing their sexuality.[10] Some 30% had actively attempted to avoid disclosure, with similar percentages feeling shame, self-blame or guilt over their practices. Many of these men have female sex partners, frequently including wives that they had married either willingly or out of a sense of social obligation.[11] Fear adverse reactions to disclosure of their MSM behaviour makes it impossible for

Global HIV Prevalence among Men who Have Sex with Men (Data display prevalence + 95% CIs)



Source: Wirtz, slide 2, from Beyer C et al. The Lancet, 2012 **380**: 367-377

them to discuss safe sex with their female lovers. It is not clear, however, whether such discussions and the resulting disclosure would lead to any reduction in HIV risk behaviour. Since HIV service agencies fear to intervene in couples' relationship for fear of losing contact with their MSM clients, they limit themselves to encouraging safe sex between MSM and frequent HIV testing. They also try to enhance their clients' ability to take the initiative in instituting safer sex practices with their female partners as well as making post-exposure prophylaxis available.

WOMEN IN A PARTICULARLY PRECARIOUS POSITION

The Indian studies portray the men as victims as much as the women. This may be true because of the special stigma attached to MSM, although the many more men engaged in extramarital relations with women face some of the same disclosure issues as MSM do, albeit without the special stigma. However the men acquire HIV, transmission from husband to wife in India represents a small but real threat (0.22% of married women test HIV-positive)[12]. Male violence within the marriage, a very common event in India as elsewhere, is associated with a four-fold increase in HIV transmission.

AIDS 2012 attendees heard that marital abuse also has a very ill effect on women's health in developed countries. The Women's Interagency HIV Study (WIHS), the largest USA cohort of HIV-positive and at-risk women, found that women in its cohort (1,642 HIV-positive and 580 HIV-negative) report partner violence at about the same rate (36%) as Indian surveys of married women in general.[13] Violence directed against the women was strongly associated with the women's death in the same year. In HIV-negative women, it raised the adjusted risk of death more than four-fold. HIV-positive women were 42% more likely to die. (The elevated risk of death among HIV-positive women as a whole probably reduced the apparent effect of male violence in this population.)

In Northern Uganda, years of warfare and forced evacuations have led to a large population of female sex workers. Researchers from the University of British Columbia (Vancouver, Canada) and The AIDS Support Organization (Gulu, Uganda) reported that these women are subject to an increasing law-enforcement clampdown.[14] They are experiencing at the same time an extraordinary amount of violence from their clients. Of the 400 sex workers surveyed by the study, two-thirds had formerly lived in evacuation camps, and their mean earnings were $50 per month. In the six months prior to the survey, 83.7% had suffered assaults by their clients, including forced unsafe sex (69% of sex workers), stabbings (29%), and rapes (19%). The heavy police presence only increased the threat. Rushed client negotiations due to nearby law enforcement personnel correlated with a 3.6-fold increase in the risk of client violence.

Client violence also was highly associated with lack of condom use. A majority of the sex workers reported difficulty in accessing condoms in any case.

The result of this hostile environment was a hyperepidemic rate of HIV (34%), a situation common to sub-Saharan Africa. The researchers concluded that the increasing criminalization and police efforts have exacerbated the HIV epidemic in northern Uganda by weakening sex workers' ability to negotiate condom use with clients.

Police in many countries, including the USA, further impede sex workers' efforts at safe sex by considering possessing condom as evidence of sex work, opening the way to further harassment as well as prosecution.[15,16] Sex workers and other women living in oppressive conditions might therefore welcome pre-exposure prophylaxis (PrEP – ART taken as protection by HIV-negative persons). PrEP attains a protection rate of up to 75% and can be taken covertly.[17]

To test this assumption, Judy Auerbach (independent consultant, San Francisco, USA) presented the results of a focus group study of USA at-risk women's attitudes toward PrEP.[18] (The study defined women as "at-risk" by virtue of their social networks, sex and drug-related risk practices, and low socioeconomic status.) The 92 focus group participants were still largely unaware of PrEP. They said that there was a need for further information on efficacy and safety from trusted sources. Nonetheless, the study concluded, the women supported establishing an affordable system for distributing PrEP to women of any HIV risk.

POLICE CRACKDOWNS ON INJECTION DRUG USERS

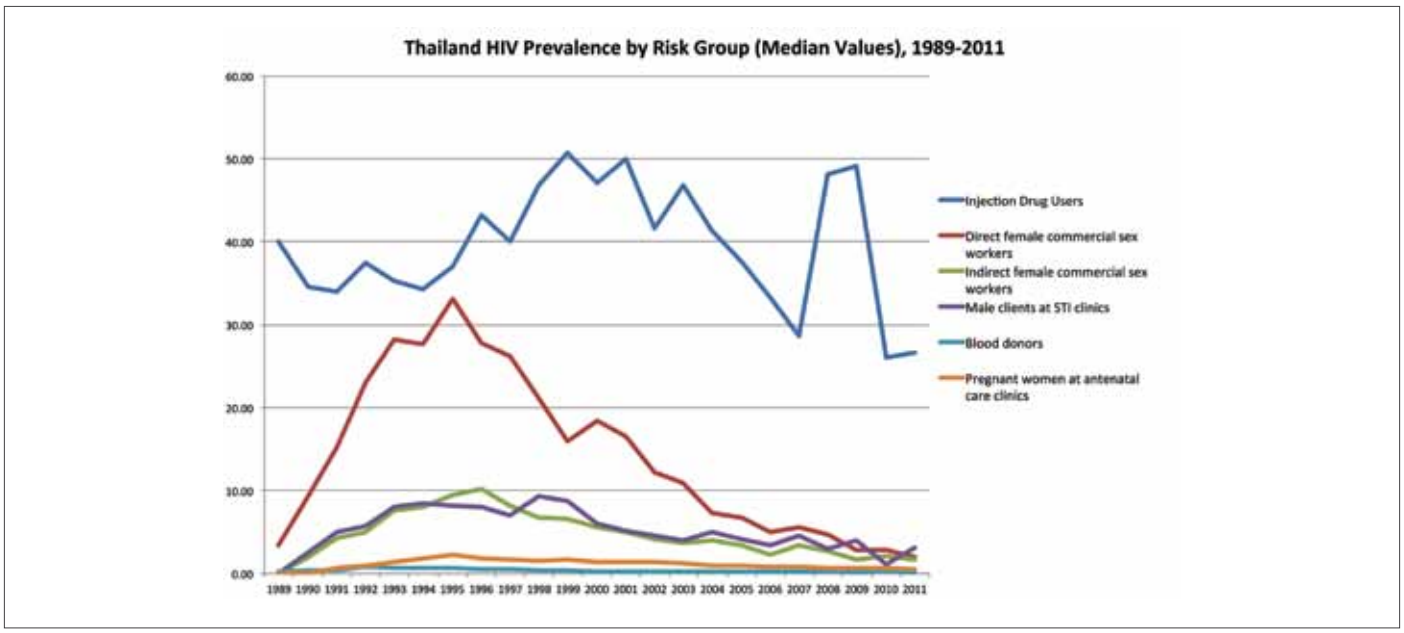
The police pursuit of injection drug users has effects similar to the criminalization of sex workers. University of British Columbia researchers along with Thai activist groups undertook a survey among Thai injection drug users that was similar to the one among northern Uganda sex workers.[19] The researchers found an upsurge in police repression over the past decade with drug users' HIV prevalence remaining extremely high (30%-50%) even as HIV rates fell in other Thai populations at high risk for HIV (see figure).

About 38% of the survey respondents said that the police had beaten them. Some 44% of respondents in the last year of the survey (2011) received beatings, and these beatings took place during police interrogations 70% of the time. According to a multivariate analysis, a higher likelihood of being the victim of police violence occurred in men, former prisoners, syringe exchange participants, drug dealers, persons younger than 37, persons with previous drug overdoses, survey respondents enrolled in 2011, and persons with poor access to health care.

The Thai study's authors concluded that the country's emphasis on a law enforcement response to injection drug use results in ongoing human rights violations by the police as well as perpetuation of the HIV epidemic among Thai drug users. They called for the implementation of social programmes objectively proven to reduce HIV among drug users. A recent international report by the Global Commission on Drug Policy came to the same conclusion.[20]

The French National AIDS Council's presentation at AIDS 2012 for these same reasons heavily criticized France's increasing prosecution and imprisonment of drug users.[21,22] French arrests for simple drug possession doubled over the first decade of

Persistent HIV Epidemic among Thai Intravenous Drug Users: Contrast with Other At-risk Populations



Source: Hayashi, MOAD0204, slide 2

this century, with much of the increase concerning marijuana possession. Prison sentences for these arrests likewise doubled and now represent 45% of all drug imprisonments. Of the 639 survey respondents, 68% reported police violence during interrogations, and 43% while being arrested.

At the same time, heroin and cocaine distribution has increased, and France's harm reduction efforts have stagnated. These harm reduction measures include allowing heroin users access to sterile syringes and opioid substitution therapies. Since their institution in 1987, these two have been largely responsible for holding HIV in check among intravenous drug users.

This criticism was further backed up in a newly published journal report by researchers from the University of California San Diego (UCSD), who described arbitrary police seizures of syringes in the possession of female sex workers active in the Mexican border cities of Ciudad Juarez and Tijuana.[23] These seizures were strongly associated with sexual abuse by the police (OR = 12.76, 95 % CI = 6.58-24.72). Thus, violence against two marginalized groups with high HIV risk comes together here.

At AIDS 2012, one of the UCSD researchers, Steffanie Strathdee (UCSD School of Medicine, La Jolla, USA) described the initial results from a randomised trial of an HIV prevention intervention targeting both unsafe drug use and unsafe sex.[24] Her group is testing this intervention, called Mujer Mas Segura (Safer Women) among injection drug-using female sex workers in Ciudad Juarez and Tijuana.[25] All study participants were required to be HIV-negative and have no other sexually transmitted diseases (STDs) at time of enrolment. The study participants received similar information in a single 60-minute session regardless of trial group. The difference was in the way the information was delivered, in either an interactive form or a traditional didactic one.

After 12 months, HIV/STD incidence decreased by more than 50% in the active safe sex training recipients compared to the didactic training recipients. The Ciudad Juarez women who received the interactive training decreased reuse of other people's syringes by 84%, compared to 71% for the didactic injection risk reduction-training recipients. Injection with used syringes declined by 95% in all the Tijuana study participants regardless of the type of training they received. The difference between the two cities may stem from the syringe distribution programmes then occurring in Tijuana but not in Ciudad Juarez.

HIV CARE AND TREATMENT LESS EFFECTIVE IN MARGINALIZED POPULATIONS

Even in a rich country like the USA, only a small proportion of persons with HIV have ART-suppressed HIV. Irene Hall (Centers for Disease Control and Prevention (CDC), Atlanta, USA) presented a government-sponsored report on the demographic factors linked to real-world response to ART.[26] The researchers found that only 33% of the total USA HIV population is on ART and that a mere 25% of the total has achieved viral suppression (undetectable viral load). The male and female rate of suppression is virtually the same, but female viral suppression exceeds the male rate after excluding MSM, who include a large affluent white fraction (see figure). Women keep up their HIV care connection more often than their male counterparts do, and their response to treatment is similar.

Major differences in treatment access in the USA revolve around race and age. Some 38% of white Americans with HIV currently receive care for the disease, 35% take ART and 30% have suppressed HIV. In contrast, 34% of black Americans currently receive HIV care, 29% take ART and only 21% have attained viral suppression. For Hispanics, the respective figures are 37%, 33% and 26%.

In regards, to age, there is a trend, at least up to age 65, for older age groups to more frequently receive HIV care and suppress their HIV (see figure). The rate of viral suppression with ART also generally increases with age: 78% for ages 18-24, 69% for ages 25-34, 73% for ages 35-44, 79% for ages 45-54, 86% for ages 55 to 64 and 84% for elderly Americans.

GROWING UP AND GROWING OLD WITH HIV

The age differences in the percentage with viral suppression reflect the challenges faced by the less resourceful age groups at either end of the spectrum. The two groups face different challenges. Adolescents and young adults tend to be alienated from the established adult world. They are initiating their own sexual and social networks and are asserting their independence from their parental families. Some are commencing their own families. They also are transitioning from paediatric to adult medical care, which expects considerably more initiative on their part.

Many of these issues could be alleviated by health services specializing in adolescents and young adults, but, as the conference heard, few such services exist.[27] Instead, adolescents frequently come across judgmental attitudes and inappropriate information, especially when trying to obtain sexual and reproductive health care. Their confidentiality is often breached, too, disrupting relationships with their families and communities.

One of the complexities of studying the needs of youth with HIV is that they are two different groups: those infected in infancy and those infected after reaching puberty. Romania represents a special case of the former because in the 1980s and 1990s it had a huge population of young children abandoned to orphanages. The paediatric medical authorities used unsterilized syringes to treat these children's multiple medical problems with ineffective microinfusions. This practice

infected 10,000 of the children with HIV, and 7,000 are still alive thanks to ART. Most of them are now 18-24 years old. According to a survey presented at AIDS 2012 by Florin Lazar (University of Bucharest, Bucharest, Romania), nearly 80% have received ART for six years or more.[28] However, their current access to HIV services is limited. Just 9.7% work, so the survey respondents are heavily dependent on government subsidies and medical services. Only 45% say they have unlimited access to ART, and the proportions claiming full access to care for other conditions is still lower. The survey respondents also showed signs of treatment fatigue. Just 59% said that they were 100% adherent in the month before the survey. These factors combined to yield a low rate of suppressed HIV – 21.2%.

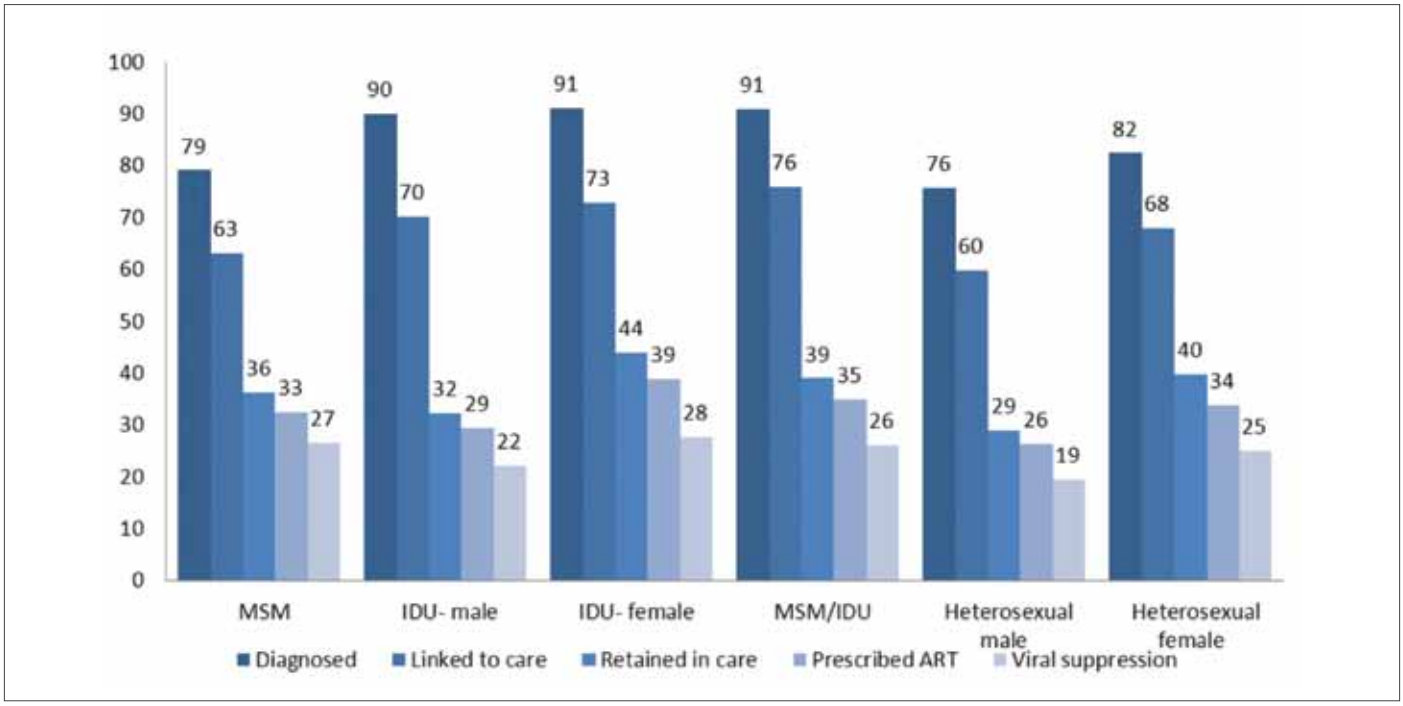
The Romanian youth had greater access to support from friends and associations for persons with HIV. A study in Nairobi, Kenya reported that this type of support was crucial to newly diagnosed youths ages 18-25.[29] These youths needed special support to chart a new identity as HIV+ individuals, reengage with their friends and community and find adequate medical and psychosocial counselling.

Social support is an important factor for older persons with HIV as well according to a survey the Terrence Higgins Trust (London, UK) conducted of patients over 50.[30,31] Many felt socially isolated and that social services were not attuned to their dual elderly/HIV status. Survey respondents reported high levels of depression and were concerned about further mental health issues. A common fear was that there would be insufficient medical and social support available to them as they aged and accumulated additional medical conditions (a phenomenon that was already occurring). They often complained of poor care or discrimination from general practitioners.

Basic to this lack of service is that HIV-positive older adults are not as well off as their HIV-negative peers. They are less often employed and depend more on government programmes. They were in addition less likely to own their homes and feared that they would end up in public old-age housing or state long-term care facilities.

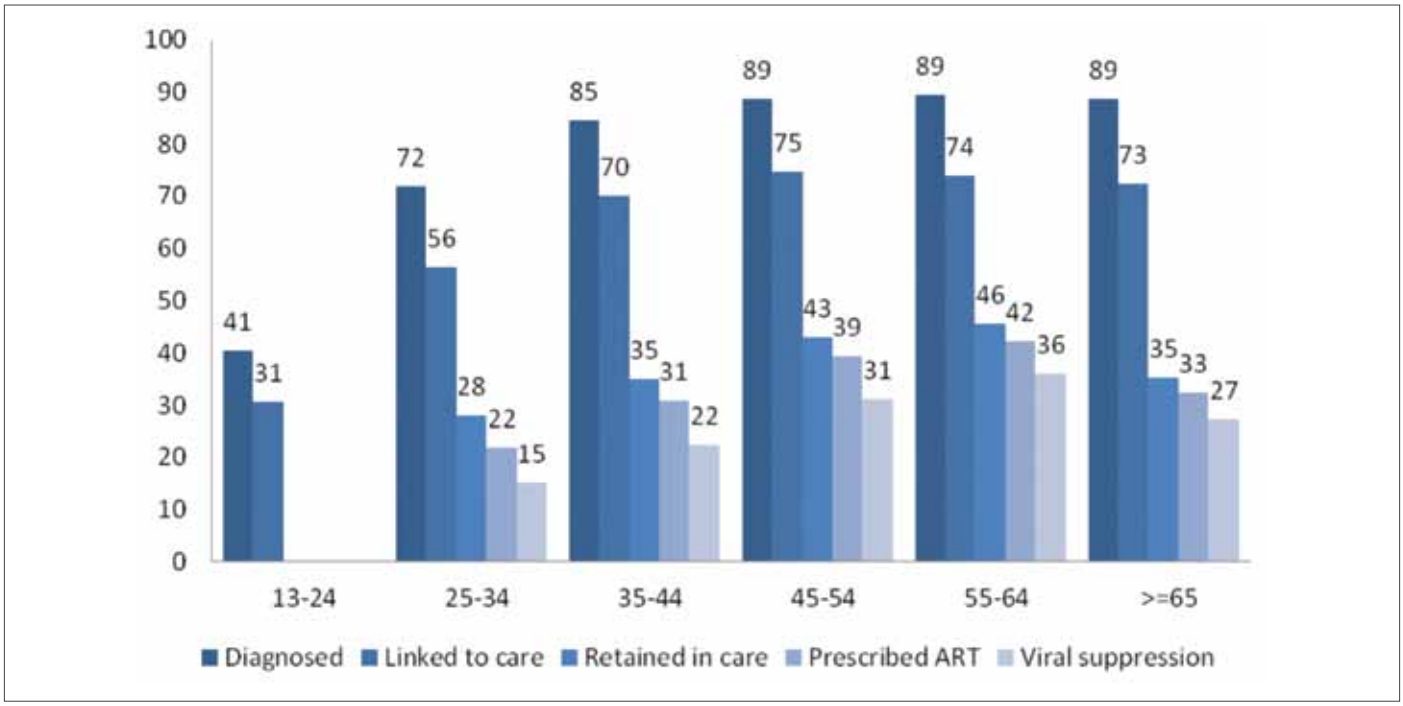
These problems were magnified in heterosexual black and other minority survey respondents compared to the heterosexual whites, but there were nuances.[32] The black and ethnic minority respondents first of all were mostly diagnosed with HIV 6-9 years ago whereas the heterosexual whites were more often either recently diagnosed or diagnosed more than ten years ago. The non-whites more often reported extreme anxiety and depression, but the whites frequently rated their mental health status as poor. The whites had much higher pill burdens than the non-whites. As a result, they more often complained about drug side effects and had adherence problems. In general, the black and minority heterosexual survey respondents had greater needs for support and help, which they tended to seek from friends with HIV, support groups, medical staff and fellow church members. Whites tended to seek support first from spouses or partners.

Percentage of Americans with HIV who Receive Care according to Risk Group



Source: Hall, FRLBX05, slide 18

Percentage of Americans with HIV Who Receive Care According to Age Group



Source: Hall, FRLBX05, slide 19.

A study presented by Rulin Hechter (Kaiser Permanente Southern California, Pasadena, USA) illustrated how the kind of depression found in the Terrence Higgins study can have a direct impact on response to HIV therapy.[33] Among 6,455 HIV patients enrolled in a large southern California health care service for at least 8 months in 2010, 51% had a history of depressive symptoms and 41% were 50 or older. Depression was independently associated with lack of retention in care (i.e. discontinuation of HIV disease monitoring). Among patients on ART, it was also a risk factor for detectable HIV on patients' last viral load assay (OR= 1.25, 95% CI=1.04-1.49). This risk of viral failure was concentrated in women (OR= 2.65, 95% CI=1.30-5.39); it did not reach statistical significance in the male patients. The implication of these findings is that depressed patients need special counselling to stay in care and adhere to ART dosing schedules. Thus, depressed elderly patients with HIV represent a need for triply specialized support services.

STRUCTURAL INTERVENTIONS: BRINGING IT ALL TOGETHER

In his conference overview of structural interventions,[34] Carlos Cáceres (Universidad Peruana Cayetano Heredia, Lima, Peru) quoted the late Jonathan Mann, who wrote, "Social marginalization, discrimination, and stigmatization, in other words a lack of respect for human rights and dignity, is itself a root cause of the epidemic." Structural interventions hope to limit HIV and support human heath by improving oppressed groups' status within their communities. They help build high-risk groups' social capital (i.e. their ability to self-organize). These interventions frequently involve sectors not directly connected to medical care, such as the educational, media, financial and political systems.

Structural projects that empower communities can be successful, as a study presented by James Blanchard (University of Manitoba, Winnipeg, Canada) found among female sex workers in southern India.[35, 36] The researchers observed that sex workers' individual and collective initiative was higher in districts where community organizations worked effectively with a multisectoral sex worker harm and HIV reduction programme. The sex workers' heightened empowerment reduced their vulnerability to attacks, raised their use of condoms and enhanced their ability to access social services.

The Blanchard group's empowerment findings stem from a small endpoint development substudy that was part of a much larger structural intervention study. Further development of analytic and measurement tools is necessary, according to the researchers. Other improvements, principally in researcher-community collaboration, also are required to advance our expertise in developing successful structural interventions.

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TRACK E: IMPLEMENTATION SCIENCE, HEALTH SYSTEMS AND ECONOMICS

SCALING UP TREATMENT TO MEET GLOBAL STANDARDS

The presentations and discussions that formed part of AIDS 2012's Track E (Implementation Science, Health Systems and Economics) were dominated by the growing international acceptance that there is one optimum world standard for HIV treatment. Accepting more restricted treatment guidelines in resource-poor settings sustains the epidemic whereas treatment in a timely fashion leads to declining HIV incidence and a return to productive life of people who otherwise would be ill and disabled. There remains a debate as to exactly what is the proper point in HIV disease for initiating therapy.

On the eve of AIDS 2012, the World Health Organization (WHO) issued a position paper with the inspiring title, The Strategic Use of Antiretrovirals to Help End the HIV Epidemic,[1] and Anthony Harries (International Union Against Tuberculosis and Lung Disease, Paris, France) summarized for the conference the WHO's evolution on HIV treatment access.[2] This process began in 2002, when the WHO issued guidelines stating that ART should be provided to all persons who had advanced HIV disease, in particular all those with CD4 counts below 200. The WHO then expanded its recommendation in 2010 to include HIV-positive patients with CD4 counts below 350, making the global guidelines similar to the standard in developed countries.

Now, the WHO is advising (though not yet officially recommending) that treatment should be available to all HIV-positive persons regardless of CD4 count who belong to specific high-risk populations. HIV is spreading rapidly in these populations and there is an urgent need to curtail the virus by reducing the infectiousness of the groups' HIV-positive members. They include serodiscordant couples (in which one member of the pair is infected and the other not), pregnant women, men who have sex with men, female sex workers and injection drug users. According to an AIDS 2012 plenary talk by Nelly Mugo (Kenyatta National Hospital, Nairobi, Kenya), these high-risk groups account for 70% of new HIV infections in her country, and the figures are similar in many other African countries.[3] Transmission within HIV-discordant couples is by far the most common avenue of transmission in these countries.

Massimo Ghidinelli, WHO PAHO, speaks at Regional Session on Latin America.
Photo: © IAS/Ryan Rayburn – Commercialimage.net

The WHO envisions further steps that would lead to a universal "test and treat" strategy in which anyone could be put on treatment as soon as they receive a positive HIV test result. This goal hinges on the dramatic results from one major clinical trial. That trial, HPTN 052, observed that early ART given to the HIV-positive member of serodiscordant couples resulted in a 96% drop in HIV transmission to the uninfected partner.[4] AIDS 2012 conference attendees heard that the HPTN 052 early treatment protocol in addition directly benefitted the HIV-positive partners by reducing their five-year rate of clinical events by 20%.[5]

Aside from its move into adult treatment as prevention, the WHO is advocating an expansion in ART to prevent mother-to-child transmission (PMTCT). WHO's proposed "option B+" would start all HIV-positive pregnant and lactating women on triple-drug ART and continue them on that treatment for life, regardless of their pretreatment CD4 count [6,7]. (WHO's 2010 guidelines recommended this option only for women with CD4 counts below 350.) The justification for option B+ is really the same as the rationale for expanding treatment in general: It enhances the prevention of HIV transmission outside of pregnancy and labour and it better protects the health of the mother.[6,7]

Malawi is the first country to adopt option B+.[7] According to a conference satellite presentation by Zengani Chirwa (Malawi Ministry of Health, Lilongwe, Malawi), the country considerably scaled up implementation of this option in the second half of 2011. It attempted to facilitate the process by integrating ART, PMTCT, family planning and mother and child health services. This integration streamlined ART procurement and supply management and centralized provider training. It also improved health service provision and patient follow-up. However, staffing and infrastructure remain inadequate for full implementation of WHO's guidelines.

ART COVERAGE IN LOW- AND MIDDLE-INCOME COUNTRIES CONTINUES TO LAG BEHIND WHO RECOMMENDATIONS

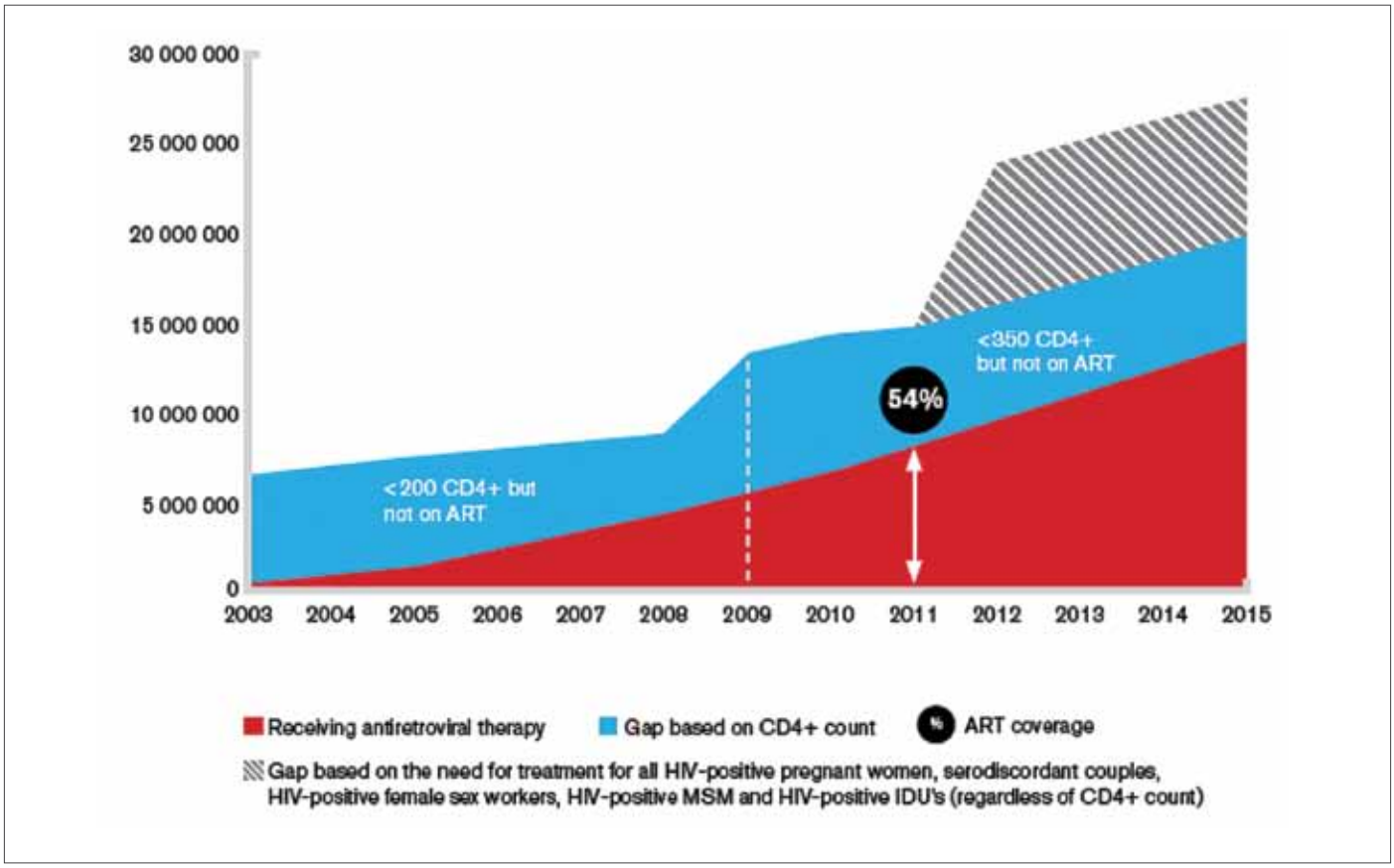
Achieving the WHO's goals will require a tremendous expansion of treatment access, which already lags far behind WHO's 2010 guidelines (see figure). In 2011, only about half the ART-eligible residents of low- and middle-income countries actually received it. A number of conference presentations considered how to meet this challenge.

Yogan Pillay (National Department of Health, Pretoria, South Africa) in his plenary address argued that only increased efficiencies will provide the financial foundation for universal access.[8] Countries will have to take the initiative to restructure their HIV services, investing their available HIV funds on the programmes that are most effective in reducing HIV mortality and incidence. The same amount of HIV spending can have vastly different results in countries following different national policies. Getting the most benefit from available funds therefore requires elaborating a detailed national plan that includes tough political choices.

Incremental savings can also be wrung from organizational reforms that ease the structural costs built into national healthcare systems. Even simple reforms can have great impact. For example, multi-month prescriptions can save valuable staff time and regularize drug supply for patients who have trouble coming to the clinic every month.

DIRECT AND INDIRECT BENEFITS OF TREATMENT SCALE-UP

Before considering the extra costs of earlier and expanded ART access, further evaluation of the benefits involved is required. These effects can be quite contradictory. Hlabisa, South Africa is one hyperepidemic district followed extensively during ART scale-up.[9] In 2004, fewer than 100 patients in the district were receiving ART although the HIV prevalence then was about 20%. The number of ART recipients has now topped 18,000. Last winter, the Africa Centre for Health and Population Studies (University of Kwazulu-Natal, Somkhele, South Africa) reported that each 1% increase in the proportion of HIV+ Hlabisa adults taking ART was associated with a 1.7% drop in the risk of acquiring HIV among the uninfected population (see figure).[10] This reduction occurred even though ART was administered very late in disease, at CD4 counts below 200 as per the initial WHO guidelines.



Source: WHO, The Strategic Use of Antiretrovirals, figure 1.

REDUCTION OF PER PERSON INFECTION RISK CAUSED BY EXPANDING ART COVERAGE IN A HIGH HIV PREVALENCE SOUTH AFRICAN DISTRICT

The 40% reduction in transmission risk that occurred over the years still leaves room for a substantial number of new HIV cases in a high-incidence area like Hlabisa. Further decreases in transmission can be expected from the current South African move to commence treatment at CD4 counts of 350 rather than 200.[11] According to an AIDS 2012 presentation, a district in Uganda that implemented early treatment saw its median viral load drop from 2,200 RNA copies/mL to below 500 copies/mL during the first year.[12] The conference also heard that in British Colombia, earlier ART accompanied by such declines in "community" viral load were associated with decreases in new HIV diagnoses.[13]

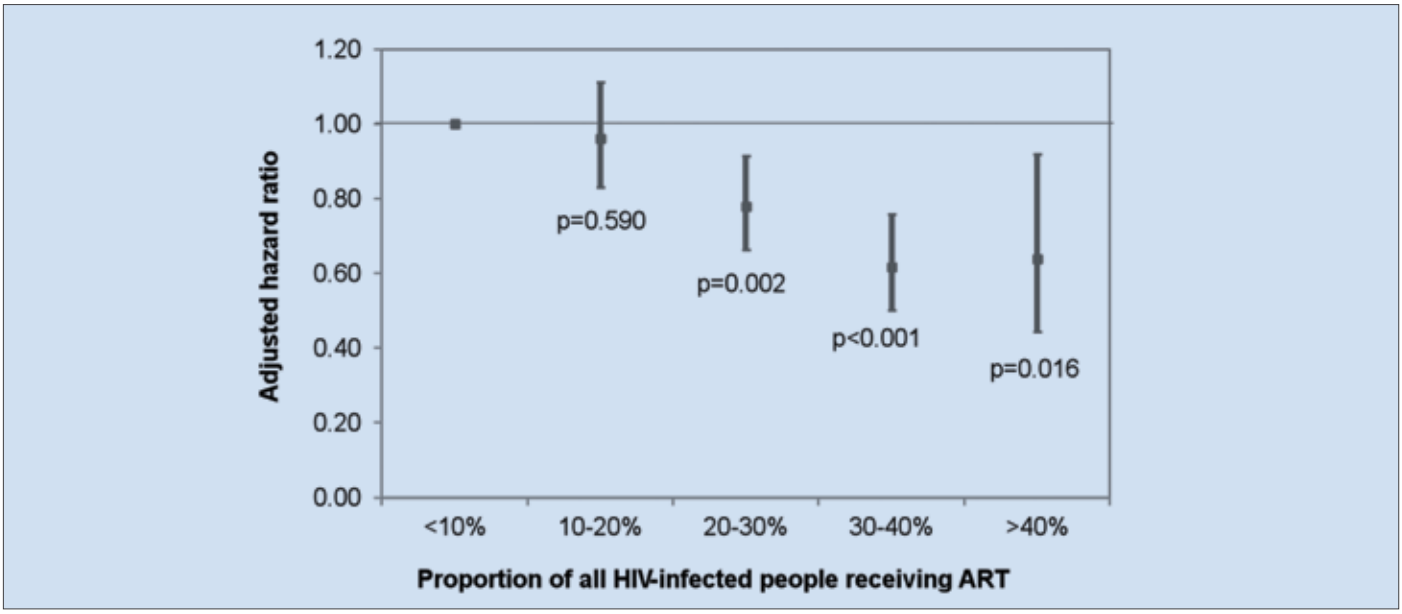
Be that as it may, the Africa Centre researchers reported that the current reduction in risk has not lasted long enough to make up for the extended lifespan of people living with HIV.[9] Instead, HIV prevalence rose to 28% during the 2004-2011 period, largely due to the expanding population of female HIV survivors above 25 years old. That is not to gainsay the benefits of added life expectancy. The researchers reported in a separate presentation that since ART has become available, the mean life expectancy of all the community's 15 year-olds grouped together – regardless of their eventual HIV status – had increased from 52.4 years to 60.6.[14] The Africa Centre researchers estimated that this 8.2-year gain is worth $26,000 to $77,000 per person, a figure that is 2-6 times higher than the individual lifetime cost of HIV treatment.

The economic value of these extra years is not abstract but real. Large numbers of Hlabisa residents gradually return to employment after they commence ART.[15,16] In their first four years of treatment, ART recipients' employment level rose from 23% to 34%, which is 90% of their pre-illness level. Once again, these gains in life expectancy and workforce participation will probably increase with the advent of earlier treatment. The potential for improvement is suggested by the large excess in mortality among 20-50 year olds. Wider ART access could restore more young adults to health and eliminate the excess deaths.[11]

The Hlabisa study was vague about its definition of "employment." A study in Malawi was more definite about the increase in work time after ART initiation, though it was vague about the time study participants had been on ART (at least 8 months) [17]. Among the Malawians who were employed prior to ART, average monthly work time increased by 43% after starting treatment, with monthly income rising by 89%. The resulting mean annual increase in earnings was $400, roughly triple the yearly cost of ART drugs.

THE COSTS OF SCALE-UP

As the calls for earlier treatment access have increased, the available international HIV funding for low-and middle-income countries has decreased. Those international funds remain essential; gains in domestic budget allocations will not be able to support adequate HIV services (see figure).



Source: Bärnighausen, MOAE0202, slide 4

SUBSTANTIAL INTERNATIONAL HIV FUNDING WILL BE REQUIRED IN SUB-SAHARAN AFRICA FOR THE FORESEEABLE FUTURE

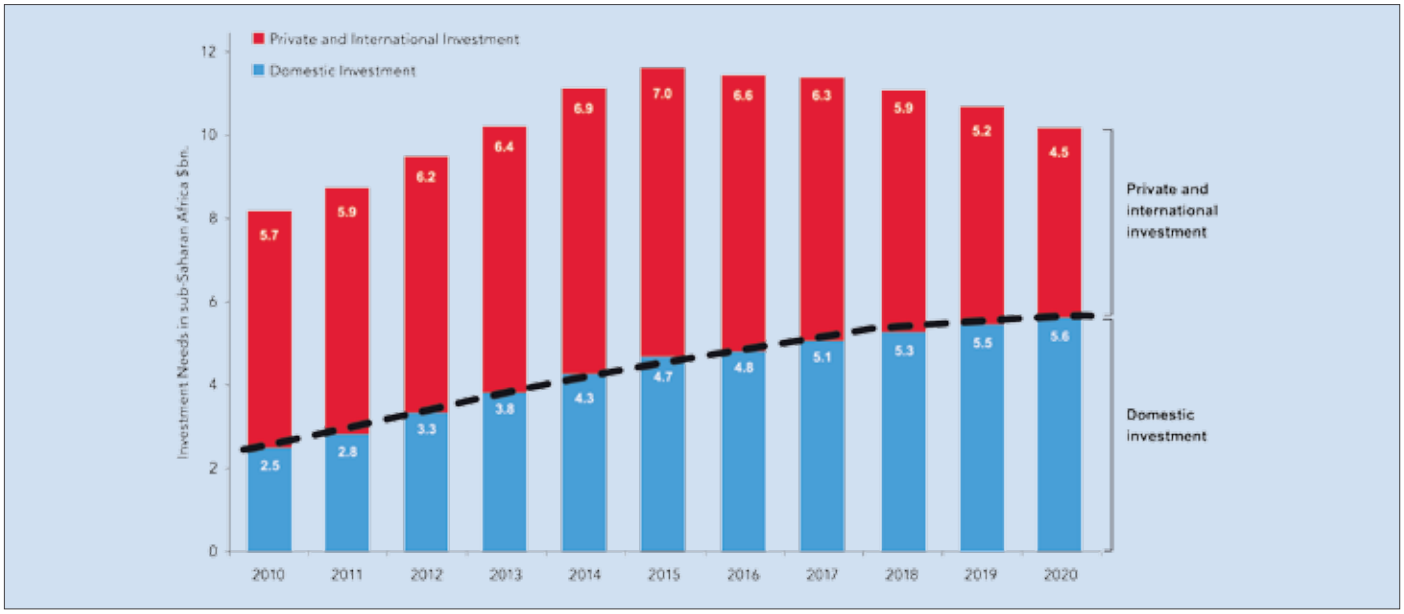
Declines in disease from earlier ART will gradually reduce funding needs over the long-term. For now, the steady decline in treatment costs has helped cushion the funding gap. Jean-Paul Moatti (INSERM, Marseille, France) tracked reported international ART sales to developing countries since 2001 in an effort to determine the factors influencing treatment costs.[18] Generic ART drugs have of course come to dominate the international market. Their constant price decreases (the latest round was announced just prior to AIDS 2012 by the Clinton Health Access Initiative[19]) have brought import prices down to less than $200 per year for first line regimens. Moatti pointed out that larger purchases are still associated with reduced costs, as is the entry of additional producers to the market.

One continuing driver of higher costs is the sharp rise since 2007 in the international prices for branded ART. The prices for these drugs increased even as their market share declined. Part of the problem is that branded-drug manufacturers increase their products' prices as they approach and pass their patent expiration dates. During this period, brand-name drug companies do not engage in price competition but instead try to establish a premium image and cost for their products. This behaviour has especially affected second- and third-line ART, for which there is relatively little generic production. Second-line regimens are 2.8 times more expensive than first-line regimens, and third-line drugs remain in the $1-2,000 per year range. This added expense continues to pose a major hurdle to comprehensive HIV care, and Moatti pleaded for maintaining a flexible intellectual property regime so that additional generic manufacturers could produce antiretroviral agents.

Of course, ART is not the only cost incurred when delivering HIV care. Upper middle-income countries also incur substantial personnel costs, but these are already low in poorer countries (see figure).[8,19] Even in the poor counties, however, health service costs can be an enormous burden.

ANNUAL CLINIC COSTS* FOR A PERSON ON ART ARE ALREADY LOW

Solomon Ahmed (USA CDC-Ethiopia, Addis Ababa, Ethiopia) provided cost projections for ramping up ART over five years [20]. These projections were part of a proposal to the USA President's Emergency Plan for AIDS Relief (PEPFAR) and mainly included the costs for clinic support services. Other expenses, including most drug costs, are paid for by the Global Fund to Fight AIDS, Tuberculosis and Malaria or the Ethiopian government. Currently, close to 400,000 Ethiopians are eligible for ART (at the country's present CD4 count threshold of 200). Some 257,000 of these patients receive treatment at present. The country enrols another 4,000 ART recipients a month, but this rate will fall short of achieving the goal of universal access over the next five years. Immediate universal access would require increasing annual expenditures from $63 million to $118 million. A slower treatment expansion would save money overall but actually cost more than immediate expansion in the last two years. At the end of the five-year period, expenses for the immediate expansion, slower expansion, or remaining at the current rate would all cost close to $120 million.



Source: Pillay, FRPL0103, slide 18

Raising Ethiopia's standard for ART eligibility to a CD4 count of 350 would require a much larger investment, though it would save money in the long-run. What about immediate ART upon diagnosis – test and treat? That would be a step too far according to an analysis presented at the conference by Till Bärnighausen (Harvard School of Public Health, Boston, USA).[21]

In Bärnighausen's model, extending circumcision to 80% of males from 45% would result in a cost of $1,086 per infection averted and $5,198 per death avoided. Choosing instead to expand ART availability by a similar proportion would cost $7,765 to prevent each extra HIV infection, with each extra death averted costing $5,741. Combining the high ART coverage and high circumcision coverage would provide more or less the same reduction in HIV as a treatment-as-prevention approach but would be much less expensive. Opting for a treatment-as-prevention effort that provided immediate ART to 80% of persons testing HIV-positive would cost $14,894 to prevent one additional HIV infection and $16,180 for each additional death prevented.

Judging by this analysis, one should wring all the benefits possible from traditional ART as per current WHO guidelines and from circumcision before embarking on a vast treatment-as-prevention campaign. Then again, Bärnighausen himself is coordinating treatment-as-prevention studies in Hlabisa. His involvement is an indication that the role of treatment-as-prevention is hardly settled.

CIRCUMCISION SLOWLY ROLLS OUT

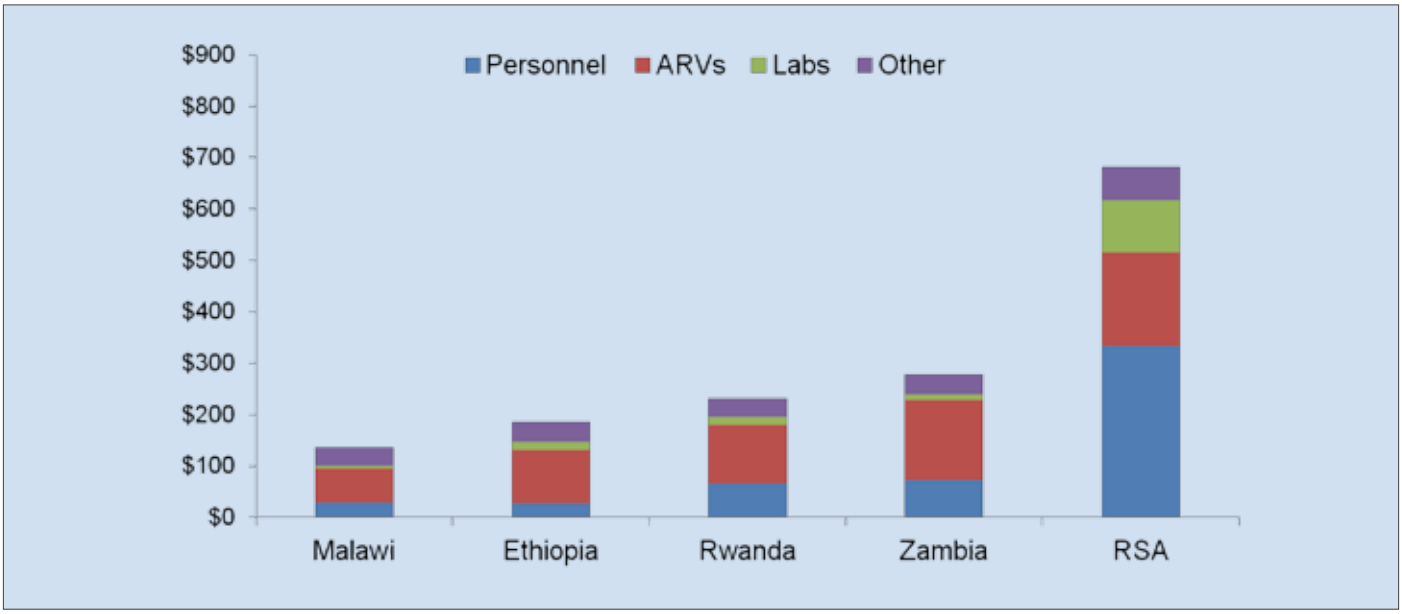
In the HPTN 052 trial, early treatment yielded a 96% decline in HIV transmission within a highly motivated and adherent group, the HIV-positive members of serodiscordant couples.[1] By contrast, pre-exposure prophylaxis (ART taken as protection by HIV-negative persons) attained a protection rate of 75% in a serodiscordant couple population and from 6% to 62% in other populations.[3] These results correlated with adherence levels to the daily antiretroviral regimen. Consistent condom use confers an 80% protection rate against HIV in heterosexual serodiscordant couples but requires great discipline.[1,22]

Male medical circumcision is the sole available intervention that does not depend on adherence – with the important exception of the required six weeks of sexual abstinence after the procedure. Over the first five years, it reduces female-to-male HIV acquisition by 57%-73%.[23,24] Widespread circumcision programmes for adults seem like the logical next step, but few countries have embarked on that route (figure).[3]

CIRCUMCISION PROGRAMMES LAG IN AFRICAN COUNTRIES

Frequent organizational issues are holding back the programmes. Physicians conducting medical circumcisions as part of public initiatives find the work demanding. They report fatigue and "burn-out" at rates reaching up to 70%.[25] According to a conference presentation by Zebedee Mwandi (CDC Kenya, Nairobi, Kenya), Kenya was able to achieve its high degree of circumcision access by task-shifting – nurses and clinical assistants rather than doctors performed 99% of 2011

*Unadjusted for confounding factors



Source: Pillay, FRPL0103, slide 11, adapted from a forthcoming Clinton Health Access Initiative/Center for Global Development report

circumcisions.[26] At the same time, the rate of adverse events arising from the procedure has declined, with nurses and clinical assistants producing an adverse event rate of 1.4%.

Niki Soboil (South African Clothing and Textile Workers Union, Cape Town, South Africa) compared two modes of circumcision service delivery in South Africa: a specialized fixed clinic in an urban district and a roving team in a rural one.[27] There was an attempt to adapt each approach to its surroundings. Still, the roving team in the countryside performed circumcisions at 60% of the cost of the urban clinic (US$ 60 vs. US$100). The rural team notably had a low follow-up rate, though.

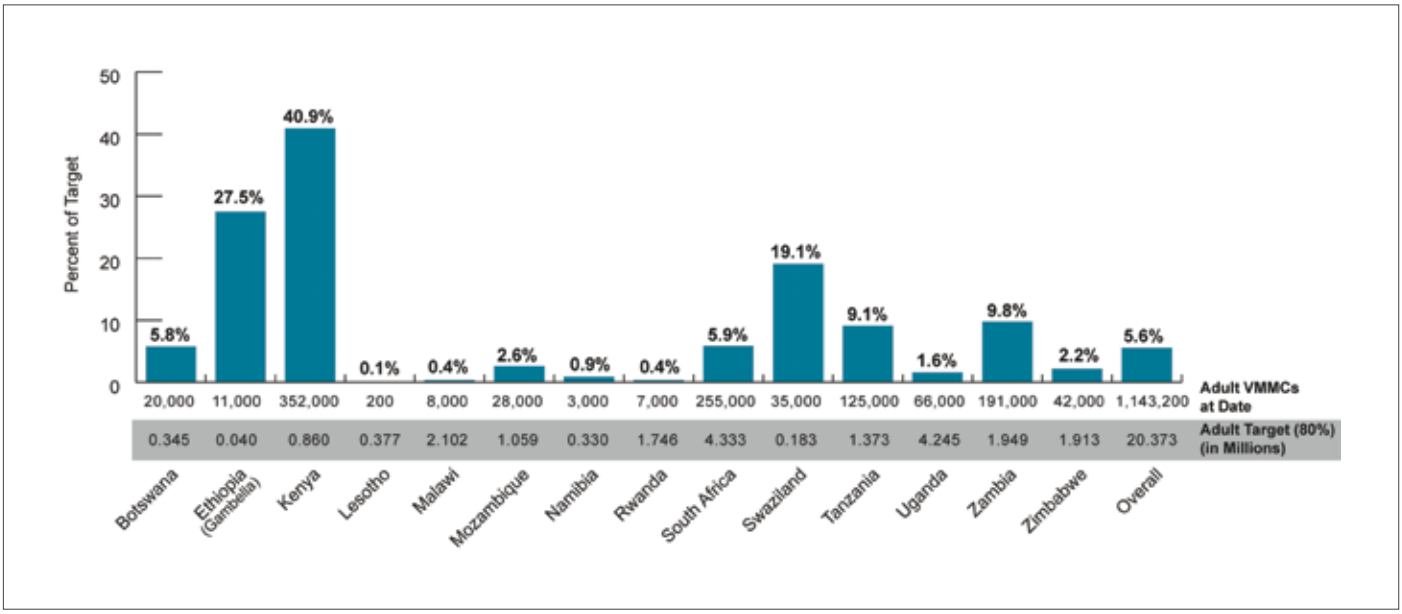
FINDING THE SYNERGIES IN COMBINED PREVENTION

Peter Cherutich (National AIDS and STD Control Program, Nairobi, Kenya) noted in a symposium discussion that although circumcision is presented as a stand-alone procedure, it is really a part of an entire prevention package.[28] Kenya designed its HIV prevention programme to include behavioural as well as biomedical interventions. Condom use continues to be a major part of the effort, which is based on counselling and testing. At the same time, the programme has the flexibility to accommodate new biomedical measures such as circumcision or pre-exposure prophylaxis in a cost-effective manner, without overhauling the programme's organization or creating parallel delivery systems.

Mean Chhi Vun (National Center for HIV, Dermatology and STI Control, Phnom Penh, Cambodia) described how similar programmatic organization in his country allows it to aspire to completely eliminate new HIV cases by 2020.[29] The country started out in 2000 with an HIV prevention programme that included condom promotion among sex workers, voluntary counselling and testing, and home-based care. It has since added universal access to ART for persons with CD4 counts below 350 and further prevention programmes targeting at-risk populations. It has also integrated tuberculosis, sexually transmitted disease and antenatal care (including PMTCT) with its HIV services, while continuing to upgrade these programmes. Since 2000, HIV prevalence has declined by 27% and estimated incidence by 90%. Measures that promise to bring these figures down even further include increases in community-based testing and counselling, stronger linkage of testing to treatment and care, and expanded use of ART in pregnant women and persons with higher CD4 counts as well as in serodiscordant couples.

Cambodia has made great strides in HIV control, but it still has far to go. Chhi Vun did not mention circumcision as part of the country's plan whereas he stressed treatment-as-prevention. Moreover, conference presentations on Cambodia found continuing deficiencies in programmes for pregnant women [30], sex workers [31] and men who have sex with men.[32] In addition, authors criticized Cambodia's police crackdowns on sex workers and drug users as a threat to HIV prevention efforts.[33] One study reported that HIV testing typically occurs late in the disease process. The mean CD4 count of people testing HIV-positive in Cambodian clinics was only 169.[34]

The Cambodian experience nonetheless illustrates the strength of combining prevention strategies, especially when resources are limited and individual initiatives cannot live up to their potential. Combined prevention – or better yet, combined prevention and treatment – represents a framework for more efficient control of the HIV epidemic.



Source: Pillay, FRPL0103, slide 11, adapted from a forthcoming Clinton Health Access Initiative/Center for Global Development report

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Leadership and Accountability

IAS Past President and AIDS 2012 International Chair Elly Katabira speaks at Kick-Off Session.

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The significance of the return of the International AIDS Conference to the USA of America after 22 years was a recurring theme throughout AIDS 2012. U.S. Secretary of Health and Human Services Kathleen Sebelius stated in the opening session of the conference that the now-repealed USA entry ban was a policy based on faulty science that ran contrary to America's deepest values. While acknowledging the importance of the USA lifting its HIV entry ban in 2009, International AIDS Society (IAS) Past President Elly Katabira pledged that the IAS will continue to campaign vigorously to change laws and policies in the 46 countries that continue to enforce travel restrictions on PLHIV.[1]

ACHIEVING AN AIDS-FREE GENERATION

There was a great deal of optimism at AIDS 2012 that HIV as an epidemic could be controlled within a generation. USA Secretary of State Hillary Rodham Clinton, who first introduced the possibility of an AIDS-free generation in November 2011, reaffirmed the commitment of the USA government to reaching this goal. Anthony Fauci of the USA National Institute of Allergy and Infectious Diseases said the world now has the scientific basis to end the HIV pandemic from an epidemiological perspective, but would not be able to do so without a sustained global commitment to implementation.[2]

Despite the optimism to end HIV as an epidemic, the fact that a cure for HIV is still not within sight was discussed by several presenters. Javier Martinez-Picado of the IrsiCaixa Foundation in Spain noted the great progress that has been made from a scientific point of view, but cautioned that viral eradication is not yet achievable.

March in Washington, D.C., during AIDS 2012.

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He added that PLHIV on antiretroviral therapy (ART) were likely to continue to develop chronic long-term conditions, such as cardiovascular complications, creating additional challenges for healthcare systems.[3] The Lancet's Richard Horton urged delegates not to allow the ambitious and hopeful vision of ending the HIV epidemic to cloud a crisis that still affects millions of people. He called out in particular a "stubborn epidemic of stigma" against gay men and women and the transgender community.[4]

The financial and logistical challenges of achieving an AIDS-free generation were the subject of many sessions. As a result of the 2011 decision by the Global Fund to Fight AIDS, Tuberculosis and Malaria to suspend Round 11 of its funding, many of the highest burden countries are scaling back plans for implementation of advances and are reviewing their ART coverage targets. Conference speakers expressed concern around the declining amounts of funding available in each round, the increasing time between funding rounds, and failure of donors to meet replenishment targets.[5]

USA President Bill Clinton noted that to achieve universal access to ART by 2015, there will need to be a 30% increase in new people on treatment each year. He also noted that the average cost to treat a person in some African nations is US$200 a year, much lower than previously thought, making the possibility of achieving the 2015 UNAIDS goal realistic, if appropriate investments in infrastructure were made.[6] Bill Gates of the Bill and Melinda Gates Foundation cited the need for increased scientific research, especially in terms of a vaccine, for the world to achieve the goal of ending the HIV epidemic.[7]

MAINTAINING POLITICAL MOMENTUM AND COUNTRY OWNERSHIP

During the AIDS 2012 Closing Session, the conference's USA Co-Chair Diane Havlir commented on the first-ever session at an International AIDS Conference on leadership from emerging economies, particularly the increased roles these countries are playing, not only in their own countries, but in the global response.[8] In the session, Jeffrey Sachs of The Earth Institute lauded the response of Brazil, China, India, and South Africa, and called upon each to share financial resources and lessons learned with poorer nations.[9] Fareed Abdullah of the South African National AIDS Council said his country will lead by example. He noted that South Africa will increase its HIV budget 15% per year for the next three years and said other countries should follow its lead.[10]

The concept of country ownership was a recurring theme in many plenary and panel discussions. Kesete Berhan Admasu, Ethiopian State Health Minister, described four essential steps to effective country ownership: inclusive planning conducted by an affected country, adequate local and international funding aligned with the plan, implementation that meaningfully involves local governments and NGOs, and mutual accountability between countries and international partners.[11]

At a special session with HIV and health ambassadors from Australia, France, Kenya, the Netherlands, Sweden, and the USA there was consensus that affected countries need to collaborate with international donors to make meaningful use of increasingly scarce resources. There needs to be a focus on greater transparency, accountability, and efficiency.[12] Kunyima Banda of Zambia addressed the issue of accountability literacy, noting that the "HIV Leadership through Accountability Programme" informed the creation of Zambia's national AIDS strategy, while strengthening the effectiveness of PLHIV as informed advocates.[13] In a skills building workshop, Penelope Saunders of the Best Practices Policy Project, presented an overview of the Universal Periodic Review, a new United Nations human rights monitoring mechanism.[14]

Walter E. Washington Convention Center.
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For resource-poor nations, country ownership will require new funding sources. Albert Manenji of the National AIDS Council of Zimbabwe discussed lessons learned from the AIDS Levy in Zimbabwe. Three percent of corporate and personal income taxes are directed to the National AIDS Trust to finance various programmes to respond to the HIV epidemic.[15]

The case for the continued commitment of developed nations was made by several presenters. USA Senator Marco Rubio stated that it was in the best interests of the USA to continue to support global efforts.[16] French Minister of Health and Social Affairs Marisol Touraine stated that France would implement a tax on certain financial transactions to increase its support of international AIDS programmes.[17] Former Spanish Vice President Elena Salgado stated the global economic crisis cannot be an excuse to pull back from supporting the international response to AIDS. She said Western countries need to continue to allocate resources where they are the most useful. She called for a new level of mutual accountability that moves beyond traditional financial responsibility to social accountability where the needs of all PLHIV are met.[18]

Numerous sessions addressed the role the private sector must play in a sustained effort to end AIDS. Rhonda Zygocki discussed Chevron's perspective that addressing HIV in the workplace by promoting access to care and HIV prevention efforts among its employees is essential to its core business.[19] Anthony Pramualratana of the Thailand Business Coalition on AIDS commented that Thailand's National Code of Practice on corporate social responsibility is based upon the International Labour Organization model, and the country was now sharing its best practices with others.[20] Partnerships are key to programme design and implementation. Paurvi Bhatt of Levi Strauss & Co. discussed Levi's strategy of leveraging partnerships with local NGOs, which has resulted in reaching employees in 40 countries. Nikki Soboil pointed out that the South African Clothing and Textile Workers Union Worker Health Program delivers free medical male circumcision to not only its workers, but also to their neighbours.[21]

Amidst the backdrop of AIDS 2012, nearly 5,000 people signed the Washington, DC Declaration, in the weeks before and during the conference. The DC Declaration calls upon the global community, with the fullest engagement of the community of PLHIV, to seek renewed urgency to expand the global AIDS fight and calls for nine concrete actions.[22]

Jurema Werneck, CRIOLA, Brazil, talks at the AIDS 2012 Regional Session on Black Diaspora.
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AIDS 2012 Regional Session on Black Diaspora.
Photo: © IAS/Deborah W. Campos – Commercialimage.net

INCLUSION OF VULNERABLE POPULATIONS IN SETTING POLICY

Many presenters, including Cheryl Overs of the Global Network of Sex Work Projects, criticized USA immigration policy denying sex workers and injecting drug users entry to the USA and called for the USA to change this policy, as well as the PEPFAR Anti-Prostitution Loyalty Oath. Paul Semugoma of the Global Forum on MSM and HIV implored leaders, especially those in Africa, to include men who have sex with men (MSM) in national HIV strategies, saying that MSM need to be stakeholders alongside politicians, researchers, and providers.[23] Mariangela Simao of UNAIDS said the global community will not reach the target of 15 million people on ART by 2015 if it does not address the underlying issues of MSM and other keys in accessing treatment.[24]

During the Red Ribbon Awards ceremony, Michel Sidibé of UNAIDS said there is still a real need to fight prejudice, stigma, discrimination, exclusion, and criminalization. He presented the first Red Ribbon Award for prevention among people who use drugs to the Afraye Sabz Association of Iran and Espolea of Mexico.[25]

At the AIDS 2012 Closing Session, Ian McKnight of the Caribbean Vulnerable Communities Coalition and Anna Zakowicz of Global Network of People Living with HIV, called the exclusion of drug users and sex workers from AIDS 2012 an "abomination." They called for greater inclusion of vulnerable populations at AIDS 2014 and other conferences.[26]

OTHER SIGNIFICANT THEMES DISCUSSED AT AIDS 2012

The involvement of youth in setting policy agendas was discussed throughout AIDS 2012.[27] New IAS President Françoise Barré-Sinoussi called upon a new generation of scientists, activists, and political leaders to join her and others at the forefront.[28] So too, the role of faith-based organizations, particularly in developing nations, was the subject of several sessions. MacDonald Sembereka of Malawi acknowledged the role some religious leaders played in stigmatizing PLHIV at the outset of the epidemic. However, he noted that many churches in Africa are now leading efforts to fight stigma and deliver healthcare and that these local efforts do not necessarily need to rely on international aid.[29]

The use of social media as an accountability tool was discussed in many sessions, including the Global Village Session, Strengthening the Global HIV Response Through Social Media: Moving Beyond the Tweets.[30] Two skills-building workshops addressed HIV and people with disabilities. Hendrietta Bogopane-Zulu of South Africa encouraged activists to continue fighting for inclusion of people with disabilities, who make up 15% of the world's population, in national strategic plans.[31]

Numerous Satellite Sessions held before and during the conference explored issues of leadership and accountability, including sessions on strengthening organizational capacity,[32] the importance of community engagement in crafting effective, local treatment solutions,[33] and Country Coordinating Mechanism oversight and Global Fund compliance.[34] Additionally, official AIDS 2012 Hubs around the world have been established to foster the development of country-level leadership skills, including Hubs in China, Uganda, and Peru.[35]

AIDS 2012 volunteers. Photo: © IAS / Steve Shapiro – Commercialimage.net

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COMMUNITY

AIDS 2012 Global Village.
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The AIDS 2012 Community Programme reaffirmed human rights as the central vehicle to end the HIV epidemic. With the science, knowledge and evidence now at hand to begin to end the epidemic, the Community Programme included sessions examining the barriers to implementing effective interventions and strategies for overcoming them. As community rapporteur Garry Brough noted,

> "What has been demonstrated again this week… is the fact that we must still fight against social injustice – against laws and judgments that not only prevent us from being who we are, but that discourage or actively prevent us from being able to access the medication and support that we need."[1]

Exhibition Area at AIDS 2012 Global Village. Photo: © IAS / Ryan Rayburn – Commercialimage.net

CRIMINALIZATION OF HIV AND MARGINALIZED GROUPS

Criminalization of HIV and marginalized groups most affected by HIV was a major focus of the conference.

Representatives of the Global Commission on HIV and the Law presented the commission's findings and recommendations, released in July 2012. The commission found no evidence that laws criminalizing HIV transmission, exposure, and non- disclosure reduce HIV transmission, but did find substantial evidence that these laws are abused to single out vulnerable people and increase stigma and discrimination, create mistrust of service providers, and prevent people from seeking HIV testing and treatment. The commission found that women face inequality in legal protections and face severe disadvantages that create increased vulnerability to HIV infection, human rights violations and violence.

In the area of intellectual property (IP) and trade agreements, the commission also found that IP laws limit treatment access and called for complete revision of the entire IP system as it relates to pharmaceutical products. The commission called for decriminalization of drug use and sex work and for reform of international narcotics conventions to bring them in line with human rights approaches.[2]

An overview of the global picture of HIV-related prosecutions provided by Edwin Bernard of the HIV Justice Network showed that the highest rates of prosecutions are in high-income countries, with the USA topping the list. In Africa, 28 countries have adopted HIV-specific laws, more than half the result of USA Agency for International Development (USAID)-funded efforts for the adoption of the 2004 "model law." Despite claims that these laws would protect women, the result has been disproportionate prosecutions of women. In Eastern Europe and Central Asia, prosecutions have been rare, while Western Europe has high prosecution rates. Some positive developments can be seen in Africa and in Western Europe, with advocacy campaigns in four African countries to remove problematic sections of criminal laws and committees in three European countries to review and revise these laws.[3]

According to examples from Canada, China, France, Macedonia and the USA, the criminalization of sex work leads to increased vulnerability of sex workers to violence, HIV and other STIs, and other harmful outcomes. Transgender women who do sex work are particularly vulnerable to violence by police, as they have little recourse because of criminalization in many countries.[4]

Criminalization and related issues of stigma and discrimination were also themes in North America and the Middle East and North Africa regional sessions, with panellists and audience members challenging governments to address high levels of HIV in key populations by addressing laws related to drug use, sex work and men who have sex with men (MSM).[5]

Communities faced with HIV-related persecutions or discrimination have responded in a variety of ways. Activists in Jamaica adopted a two-pronged strategy to fight "buggery" laws using international laws/agreements to bring a challenge in the Inter-American Court of Human Rights while engaging in domestic mobilization and education campaigns. A broad coalition of HIV, women's, human rights, and other groups in Namibia mobilized a dual track of litigation and advocacy to combat involuntary sterilization of women living with HIV. In the USA state of Louisiana, grassroots advocates partnered with legal advocates to successfully challenge through the courts and legislature the state's "crimes against nature" law, which was selectively enforced against sex workers, LGBT people, and poor women[6].

In his plenary talk *Turning the Tide for MSM and HIV*, Paul Semugoma drew the correlation between both the criminalization of homosexuality and the "huge denial" that MSM even exists and the dearth of prevention services for MSM in many places. "Less and less gets to the MSM because of the stigma, because they are criminals."[7] The Regional Session on Eastern Europe and Central Asia illustrated how punitive laws on drug use and refusals to implement harm reduction strategies lead to the region's status as the area in the world where the epidemic is increasing most rapidly.[8]

Nikos Dedes, EATG, speaks at the Community Scientific Literacy Workshop during the Towards an HIV Cure pre-conference symposium.
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Nitasha Kumar, with Sharon Lewin, Françoise Barré-Sinoussi and Jean-Francois Delfraissy, receives the IAS-ANRS Young Investigator Award at the Towards an HIV Cure pre-conference symposium.

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HIV ENTRY BARRIERS FOR SEX WORKERS AND PEOPLE WHO USE DRUGS

An example of the barriers and challenges facing sex workers and People who use drugs was highlighted well before AIDS 2012 convened. USA entry restrictions on both groups meant that many from outside the USA would be unable to attend the conference. The restrictions led to calls by some for the relocation of the conference and subsequent extensive efforts to find alternative means for their participation.

Just prior to AIDS 2012, and with the support of the conference secretariat, the Eurasian Harm Reduction Network (EHRN) hosted a forum in Kiev, Ukraine to prepare messages from representatives from the drug-using communities in the Baltic states, Belarus, Georgia, Russia, Ukraine, and Uzbekistan to the delegates of AIDS 2012. Forum participants took part in panel discussions and created video messages that were played at a conference plenary session and expressed their strong desires to be present and active in the conference to bring their voices to discussions about the issues that affect their lives. EHRN will host a post-conference hub in September 2012 to follow up on the forum.

During the week of the conference, more than 500 sex workers from 41 countries attended a conference hub in Kolkata, India, known as the Sex Worker Freedom Festival. The meeting drew attention to women's health and reproductive rights, as well as the USA entry restrictions, and received significant media coverage. Several AIDS 2012 sessions featured live links with the Kolkata hub.

HUMAN RIGHTS AND BIOMEDICAL PREVENTION STRATEGIES

Effective biomedical strategies were recognized as showing great promise in preventing onward transmission and reducing community viral load, but the need to protect and strengthen human rights was a recurring theme in relation to how these strategies would need to move forward.

Accountability and genuine community engagement and partnership in designing, implementing and disseminating research trials and prevention strategies were highlighted in a number of sessions, echoing Sir Elton John's call for a humane and compassionate response that includes those communities which are most affected throughout the world and who are often the most disenfranchised and marginalized.[9]

While expressing their support for the possibilities that HIV treatment as prevention provides for increasing access to higher standards of health, panellists from Southern and Eastern Africa speaking at Human Rights and Treatment as Prevention: An African Perspective also stated strong concerns about potential for human rights violations that can arise. Concerns included coercive measures against people living with HIV to take ART primarily for public health benefits or to please a partner and

mandatory testing campaigns, as well as increased risk for HIV and other STIs among women if male partners become too confident and engage in higher risk behaviour. Issues of sustaining treatment were discussed in relation to stock-outs, lack of diagnostic tools, and long waiting lists of people who need treatment.[10]

In her plenary address, Cheryl Overs echoed similar concerns related specifically to sex workers. "I haven't raised these issues about new prevention technologies to suggest that they can't work for sex workers. I raised them to illustrate that they create challenges that can't be solved without strong inputs from sex worker advocates, and to underline the fact that the fewer rights sex workers have, the less chance we have of these new scientific developments being successful."[11]

ALTERNATIVE FUNDING SOURCES

The decision by the Global Fund to Fight AIDS, Tuberculosis and Malaria in late 2011 to suspend Round 11 of its funding is having a detrimental impact on HIV services and brought a tremendous amount of urgency to discussions about developing new, on-going and stable funding sources for global HIV and AIDS initiatives.

Activists dressed as Robin Hood, urged the adoption of a financial transaction tax, often referred to as a "Robin Hood tax." Models suggest that .0005% of the world's financial transactions could produce US$300 billion per year.[12] In a video announcement at a conference plenary session, French President François Hollande announced that France would implement a tax on financial transactions as an innovative financing instrument, and Marisol Touraine, France's Minister of Health and Social Affairs, later stated that France will continue to be actively engaged with its European Union and international partners to establish a tax on financial transactions.[13]

In his remarks to the closing session, USA President Bill Clinton cited the success of UNITAID, which has saved hundreds of thousands of lives, as an important and innovative funding mechanism.[14] UNITAID's nine-country air ticket levy has raised about $US9 billion over the last five years.[15] President Clinton called for additional innovative financing schemes, noting that the International Finance Facility for Immunizations may offer a good model.[16]

Beyond funding schemes, speakers and delegates also called for governments and drug manufacturers to ensure that patent laws and restrictive pricing do not inhibit the effective global rollout of life-saving medications. They also called for the political will to strengthen health infrastructures to deliver ART to ensure that no child is born with HIV.

Fred Verdult, Netherlands, talks at the Towards an HIV Cure pre-conference symposium.
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YOUTH LEADERSHIP

Young people are key to moving towards the goal of an AIDS-free generation and a number of sessions dealt with the issues they face both in terms of living with HIV and seeking to prevent new infections. Comprehensive sexual, reproductive health and relationship education was identified as strongly needed. In many African countries, research showed that whilst HIV prevention services and testing opportunities were often widely available, sexual and reproductive health information was far more limited. This is a particular issue for young women and girls, who may have limited power and decision-making abilities within sexual relationships and little or no access to family planning.[17]

The difficulties of HIV disclosure to partners and anxiety about stigma and discrimination if status was revealed were significant issues for young people. Interactive youth-led workshops sought to address some of the issues and provide tools and strategies to facilitate the process and skills building that young people need to manage disclosure in a way that is as comfortable and safe as possible.[18]

AIDS 2012 Exhibition Area. Photo: © IAS/Steve Shapiro – Commercialimage.net

COMMUNITIES AND INDIVIDUALS DRIVING CHANGE

While global and national responses are key to removing legal and structural barriers, the need to work for change at the personal level is equally crucial. Several sessions showcased tools to advocate for this change and for the greater involvement of people living with HIV and key-affected populations. These ranged from policy and advocacy resource tools to the use of social media to inform and educate, to challenge stigma and discrimination, and to effect change.

The participation of affected communities at AIDS 2012 was pronounced. In a first at an International AIDS Conference, the Black Diaspora Working Group, chaired by the African and Black Diaspora Global Network on HIV and AIDS, organized a session that focused on priorities and action plans to address the need for a coordinated global HIV framework for Black Diaspora populations.[19] A panel of researchers and community members involved in research with gay, bisexual, and other MSM presented newly-created guidance on conducting HIV research with these communities in rights constrained environments. At the session, researchers and community members shared case studies from research conducted in Swaziland, Peru, and Ethiopia.[20] Community members led and participated in many other sessions, including discussions around improving the number and quality of HIV healthcare workers[21] and building a political voice to address sexual reproductive health and rights for women living with HIV.[22]

Brough noted the importance of meaningful participation of affected communities in the on-going response to the HIV epidemic. "Claiming equality also means claiming a place at the table where the changes that affect us are decided, be they political or clinical."[23] Success in this arena requires affected communities to continue to speak out, honestly and loudly and in his plenary address Phill Wilson challenged the community to take responsibility, ownership and leadership – a challenge that many accepted with passion throughout the conference.

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