Welcome to the 96th issue of *HIV This Week*! In this issue, we cover the following topics:

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   - Bisexual behaviour in China: a first meta-analysis  
   - Lower levels of bisexuality in peri-urban Cape Town

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Don’t forget that you can find a wealth of information on the HIV epidemic and responses to it at www.unaids.org.
1. Bisexuality in men who have sex with men

Prevalence of bisexual behaviour among bridge population of men who have sex with men in China: a meta-analysis of observational studies


Yun and colleagues aimed to integrate empirical estimates of bisexual behaviour among the bridge population of men who have sex with men in China and their HIV and syphilis prevalences stratified by sexual behaviour. Pubmed, Chinese Biomedical, Chinese National Knowledge Infrastructure, VIP, Wanfang and Google Scholar databases were searched to January 2011 to identify relevant articles. Data for eligible citations were extracted by two reviewers. All analyses were performed using Stata 10.0. Forty-nine articles (including 28,739 study subjects who were men who had sex with men) met the selection criteria. Aggregated findings indicated that the estimated prevalence of bisexual behaviour among men who have sex with men in China is 31.2% (95% CI 28.1% to 34.5%). HIV and syphilis prevalences were 5.4% and 11.4%, respectively, among men who have sex with men engaging in bisexual behaviour and 3.8% and 9.3% among those who were only having sex with men. HIV prevalence among men who have sex with men engaging in sex with both men and women was significantly higher than in those who were only having sex with men (OR 1.30; 95% CI 1.04 to 1.62; p=0.02). There is a high prevalence of bisexual behaviour among men who have sex with men in China and bisexual behaviour is significantly associated with increased HIV infection risk. The results of this meta-analysis highlight a critical pattern of HIV transmission among men who have sex with men in China and indicate that targeted interventions aimed at encouraging safe sex practices and promoting societal and family acceptance of men who have sex with men are urgently needed.


Editor's note: In mainland China, the proportion of HIV infections attributed to sexual transmission between men rose from 12% in 2007 to 35% in 2009. This first-ever meta-analysis of bisexual behaviour among Chinese men was based on 49 articles (from 53 unique studies) that met the selection criteria. About 30% of men who had sex with men also reported sex with a woman in the previous 12 months. These men were 30% more likely to have HIV infection than those who did not report sex with a woman. This finding is somewhat counter-intuitive for those who use terms like ‘bridge population’ to suggest that higher HIV prevalence in one key population can place the so-called ‘general population’ at risk. In this case, the bridge is from where to where? With homosexuality still highly stigmatised in a cultural context that emphasises social standing, it is unclear how meeting family expectations to marry women could increase HIV risk for men who have sex with men. The value of this study is that it is hypothesis-generating. It spotlights the need for ethnographic and other qualitative studies to explore the factors that place bisexual men at higher risk of HIV than their ‘men only’ counterparts. Engaging these men to learn more about their experiences and using their voices to inform HIV prevention programming could help prevent HIV from spreading further among men who have sex with men and their female partners in China.

HIV risk and associations of HIV Infection among men who have sex with men in peri-urban Cape Town, South Africa


The HIV epidemic in sub Saharan Africa has been traditionally assumed to be driven by high-risk heterosexual and vertical transmission. However, there is an increasing body of data highlighting the disproportionate burden of HIV infection among men who have sex with men in the generalized HIV epidemics across of southern Africa. In South Africa specifically, there has been an increase in attention focused on the risk status and preventive needs of men who have sex with men both in urban centers and peri-urban townships. The study presented here represents the first evaluation of HIV prevalence and
associations of HIV infection among men who have sex with men in the peri-urban townships of Cape Town. The study consisted of an anonymous probe of 200 men, reporting ever having had sex with another man, recruited through venue-base sampling from January to February, 2009. Overall, HIV prevalence was 25.5% (n = 51/200). Of these prevalent HIV infections, only 6% of men who have sex with men who were found to be of HIV-1 positive were aware of their HIV status (3/50). 0% of men reported always having safe sex as defined by always wearing condoms during sex and using water-based lubricants. Independent associations with HIV infection included inconsistent condom use with male partners (aOR 2.3, 95% CI 1.0-5.4), having been blackmailed (aOR 4.4, 95% CI 1.6-20.2), age over 26 years (aOR 4.2, 95% CI 1.6-10.6), being unemployed (aOR 3.7, 95% CI 1.5-9.3), and rural origin (aOR 6.0, 95% CI 2.2-16.7). Bisexual activity was reported by 17.1% (34/199), and a total of 8% (16/200) reported having a regular female partner. Human rights violations were common with 10.5% (n = 21/200) reporting having been blackmailed and 21.0% (n = 42/200) reporting being afraid to seek health care. The conclusions from this study include that there is a high risk and underserved population of men who have sex with men in the townships surrounding Cape Town. The high HIV prevalence and high risk sexual practices suggest that prevalence will continue to increase among these men in the context of an otherwise slowing epidemic. These data further highlight the need to better characterize risk factors for HIV prevention and appropriate targeted combination packages of HIV interventions including biomedical, behavioural, and structural approaches to mitigate HIV risk among these men.


Editor’s note: HIV prevalence studies among men who have sex with men have been conducted in many countries in eastern and southern Africa, mostly in major urban centres. This study recruited a convenience sample of men who have sex with men, rather than a probability-based sample, in relatively clandestine gay venues in the townships around Cape Town. This limits the generalizability of the findings but they are nonetheless valuable for planning combination prevention programmes for this population. Levels of active bisexuality (past 6 months=17%) and bisexual concurrency (stable relationships with both a man and a woman=3%) were lower than those reported in other SADC (Southern African Development Community) countries, possibly due to the better social and legal contexts for gay men in South Africa. However, HIV prevalence was double that of men who have sex with men in urban Cape Town. A disconnect between constitutional protections and daily life in these townships was evident with 24% of participants reporting at least one human rights violation (e.g. denial of housing or healthcare, having been blackmailed, having been beaten by police or a government official based on their sexuality). Clearly, structural interventions to build social capital and address human rights violations, particularly those perpetrated by police, health care workers, and officials, must accompany behavioural and biomedical interventions for men who have sex with men in these townships.

2. Ageing and HIV

What do we know about older adults and HIV? A review of social and behavioural literature


The fastest growing segment of the USA HIV population is people aged 50 and older. This heterogeneous group includes people with diverse pathways into HIV-positive status in later life, including aging with the disease as well as later life-acquired infections. As people with HIV live into older ages, solving problems of successful secondary prevention and ongoing treatment requires more specific knowledge of the particular aging-related contextual sociocultural, psychosocial, and personal factors salient to the situations of persons living with HIV. Greater knowledge of these factors will help solve challenges to reducing psychological burden and promoting health maintenance for people with HIV. Yet, the current literature on aging and HIV remains nascent. To assess the state of knowledge of the sociocultural and behavioural factors associated with aging with HIV, Sankar and colleagues conducted a systematic critical
content review of peer-reviewed social and behavioural research on aging and HIV to answer the question, "How have older age, and social, cultural, and behavioural aspects of the intersection of HIV and age been addressed in the literature?" They searched First Search, Proquest, Psych Info, Pub Med, Wilson Select Plus, and World Cat and identified 1549 articles. They then reviewed these to select peer-reviewed articles reporting results of research on the social and behavioural aspects of living with HIV at age 50 and older. Fifty-eight publications were identified that met study inclusion criteria. While few publications reported clear age-related differences, there were significant ethnic differences in living with HIV in later life and also differences among older people when groups were defined by mode of transmission. Findings are discussed in light of constructs from gerontology which may contribute to clarifying how later life, life course stage, and psychological development intersect with, influence, and are influenced by HIV disease and long-term anti-retroviral therapy use.


Editor's note: Some have estimated that by 2015, 50% of all people living with HIV in the USA will be 50 years of age or older, as antiretroviral therapy extends people’s life spans and new infections continue in this age group. In 2007, 15% of new HIV infections in the USA were among people aged 50 years and older. Other reviews have addressed the interactions between biological aging, HIV disease processes, and antiretroviral therapy. This literature review focuses on how life course stage (socially-constructed expectations, eras, and transitions) and psychological development stage (e.g. capacity to adapt to changing demands) complement chronological age (the body’s biological age) in our understanding of aging and HIV. It reviews the diverse settings and conditions of the lives of older American adults living with HIV (ethnicity, mode of HIV acquisition, income, social support, etc.) and their experiences with disclosure, stigma, and ageism. Stereotypes of asexuality in the 50+ age group, held by health care providers, policy makers, and the public, delay diagnosis and treatment initiation and do not address HIV prevention needs with age-appropriate information and counselling. Beyond the biological aspects of aging and of HIV Infection, complex social, physical, economic, cultural, and psychological interrelationships influence the resilience and strengths of people in not only coping with HIV but in accomplishing their own life stage specific goals and aspirations.

3. Microbicides

First phase 1 double-blind, placebo-controlled, randomized rectal microbicide trial using UC781 gel with a novel index of ex vivo efficacy


Successful control of the HIV pandemic requires reduction of HIV-1 transmission at sexually-exposed mucosae. No prevention studies of the higher-risk rectal compartment exist. Anton and colleagues report the first-in-field Phase 1 trial of a rectally-applied, vaginally-formulated microbicide gel with the RT-inhibitor UC781 measuring clinical and mucosal safety, acceptability, and plasma drug levels. A first-in-Phase 1 assessment of preliminary pharmacodynamics was included by measuring changes in ex vivo HIV-1 suppression in rectal biopsy tissue after exposure to product in vivo. HIV-1 seronegative, sexually-abstinent men and women (N=36) were randomized in a double-blind, placebo-controlled trial comparing UC781 gel at two concentrations (0.1%, 0.25%) with placebo gel (1:1:1). Baseline, single-dose exposure and a separate, 7-day at-home dosing were assessed. Safety and acceptability were primary endpoints. Changes in colorectal mucosal markers and UC781 plasma drug levels were secondary endpoints; ex vivo biopsy infectibility was an ancillary endpoint. All 36 subjects enrolled completed the 7-14 week trial (100% retention) including 3 flexible sigmoidoscopies, each with 28 biopsies (14 at 10 cm; 14 at 30 cm). There were 81 Grade 1 adverse events (AEs) and 8 Grade 2; no Grade 3, 4 or procedure-related AEs were reported. Acceptability was high, including likelihood of future use. No
changes in mucosal immunoinflammatory markers were identified. Plasma levels of UC781 were not detected. Ex vivo infection of biopsies using two titers of HIV-1(BaL) showed marked suppression of p24 in tissues exposed in vivo to 0.25% UC781; strong trends of suppression were seen with the lower 0.1% UC781 concentration. Single and 7-day topical rectal exposure to both concentrations of UC781 were safe with no significant adverse events (AEs), high acceptability, no detected plasma drug levels and no significant mucosal changes. Ex vivo biopsy infections demonstrated marked suppression of HIV infectibility, identifying a potential early biomarker of efficacy. (Registered at ClinicalTrials.gov; #NCT00408538).


Editor’s note: One has to respect the altruism of these 36 study subjects and their perseverance – they all completed the study. They were HIV-negative men (n=26) and women (n=10), with a history of consensual receptive anal intercourse at least once in their lives. They were willing to be sexually abstinent from rectal sex for 1 week prior to treatment and for 1 week before and 1 week after each of 3 sigmoidoscopies. The latter involved a preparatory enema and biopsies of colonic tissue (28 to be precise). The results of this study have advanced the topical PrEP [microbicide] field by a leap. This is not because the product UC781 has promise. In fact, further development is not being pursued because of its stability, solubility, and other reasons. Rather, for the first time, an ex vivo (outside the body) biomarker of efficacy was used to test how well a rectal microbicide could block HIV infection. The biopsy specimens of participants in the UC781 groups (particularly those in the 0.25% concentration group) had enough of a UC781 tissue concentration from pre-biopsy topical application to suppress HIV infection of the tissue. Rectal HIV transmission is 20-200 times more likely than vaginal transmission, possibly as a result of the rectum’s single-cell epithelial lining and resident activated immune cells, combined with the risk of trauma with inadequate lubrication. The development of an acceptable, safe, and efficacious rectal microbicide is on the pathway to the long-term goal of a combination microbicide that can be used in both sexual compartments (vagina and rectum).

4. Point of care testing
Detecting drug-resistant tuberculosis: the importance of rapid testing


Despite numerous intervention strategies, including the direct observed short-course treatment strategy and improved diagnostic methods, the incidence of multidrug-resistant and extensively drug-resistant tuberculosis (TB) continues to rise globally. Many treatment policies are based on the model that acquisition of drug resistance in already infected individuals drives the drug-resistant TB epidemic, hence the focus on drug-resistance testing of retreatment cases. However, molecular epidemiology and mathematical modelling suggest that the majority of multidrug-resistant TB cases are due to ongoing transmission of multidrug-resistant strains. This is most likely the result of diagnostic delay, thereby emphasizing the need for rapid diagnostics and comprehensive contact tracing, as well as active case finding. Current diagnosis of TB in low-income, high-burden regions relies on smear microscopy and clinical signs and symptoms. However, this smear-centred approach has many pitfalls, including low sensitivity in HIV patients and children, the inability of smear to reveal drug-resistance patterns, and the need for sampling on consecutive days. In order to address these limitations, efforts have been made to expand access to Mycobacterium tuberculosis culture and drug susceptibility testing. However, the slow growth rate of the causative agent, M. tuberculosis, contributes to significant diagnostic delay. Molecular-based diagnostic methods, targeting mutations that are known to confirm drug resistance, are capable of significantly reducing diagnostic delay. Two such methods, the line-probe assay and the real-time PCR-based Xpert® MTB/RIF assay, have been described. The latter test shows particular promise for smear-negative and extrapulmonary specimens. This may prove especially useful in settings where co-infection
rates with HIV are high. However, since most research focuses on the performance of both of these assays, further investigations need to be done regarding the impact of the routine implementation of these assays on TB control programs and the cost effectiveness thereof.


Editor's note: Over two-thirds of multi-drug resistant tuberculosis (MDR-TB) cases are now believed to result from ongoing transmission of drug resistant virus rather than from acquiring drug resistance while being treated. Detecting this resistance at the time of TB diagnosis so that treatment regimens can be adjusted not only saves lives, it can save time and money while preventing onward transmission. This article tracks the development of molecular-based diagnostic methods leading to WHO’s recommendation in December 2010 to use the Xpert™ MTB/RIF real-time PCR (polymerase chain reaction) assay to detect simultaneously TB and resistance to rifampin, a key first-line TB drug. With countries such as South Africa introducing Xpert™ widely, it is time to determine the most cost-effective ways to use these new tools. The first step is to study the impact of routine implementation on treatment decisions and, most importantly, on treatment outcomes. In particular, will additional testing be needed for people living with HIV who have negative Xpert™ results since the test can miss 30% of smear-negative, culture-positive specimens? Operations research, phased implementation research and trials, and health economics studies are all needed – and the opportunity to conduct them is now.

Effect of point-of-care CD4 cell count tests on retention of patients and rates of antiretroviral therapy initiation in primary health clinics: an observational cohort study


Loss to follow-up of HIV-positive patients before initiation of antiretroviral therapy can exceed 50% in low-income settings and is a challenge to the scale-up of treatment. Jani and colleagues implemented point-of-care counting of CD4 cells in Mozambique and assessed the effect on loss to follow-up before immunological staging and treatment initiation. In this observational cohort study, data for enrolment into HIV management and initiation of antiretroviral therapy were extracted retrospectively from patients' records at four primary health clinics providing HIV treatment and point-of-care CD4 services. Loss to follow-up and the duration of each preparatory step before treatment initiation were measured and compared with baseline data from before the introduction of point-of-care CD4 testing. After the introduction of point-of-care CD4 the proportion of patients lost to follow-up before completion of CD4 staging dropped from 57% (278 of 492) to 21% (92 of 437) (adjusted odds ratio [OR] 0·2, 95% CI 0·15-0·27). Total loss to follow-up before initiation of antiretroviral treatment fell from 64% (314 of 492) to 33% (142 of 437) (OR 0·27, 95% CI 0·21-0·36) and the proportion of enrolled patients initiating antiretroviral therapy increased from 12% (57 of 492) to 22% (94 of 437) (OR 2·05, 95% CI 1·42-2·96). The median time from enrolment to antiretroviral therapy initiation reduced from 48 days to 20 days (p<0·0001), primarily because of a reduction in the median time taken to complete CD4 staging, which decreased from 32 days to 3 days (p<0·0001). Loss to follow-up between staging and antiretroviral therapy initiation did not change significantly (OR 0·84, 95% CI 0·49-1·45). Point-of-care CD4 testing enabled clinics to stage patients rapidly on-site after enrolment, which reduced opportunities for pretreatment loss to follow-up. As a result, more patients were identified as eligible for and initiated antiretroviral treatment. Point-of-care testing might therefore be an effective intervention to reduce pretreatment loss to follow-up.


Editor's note: The rate of loss to follow-up after antiretroviral therapy initiation in resource-constrained settings can be high in the first year but it is nowhere near as high as the loss to follow-up after HIV diagnosis and before treatment initiation. Weak referral links, distances to be travelled to clinics, and high mortality are important reasons. This is the first study to assess whether a diagnostic test could reduce pre-
treatment losses to follow-up and the results are resounding. Point-of-care CD4 count using a fingerpick sample replaced a system in which blood samples were sent once a week for testing (median 10 days), patients returned for a staging visit once the results became available (median 17.5 days), and each part of this process took place at a different site (HIV testing, CD4 count blood draw, and staging consultation). 30% of patients had their CD4 test done on the same day they learned they had HIV infection and by 5 days, 90% had received point-of-care CD4 testing. 50% of patients were able to have their staging consultation on the day they completed CD4 count testing. About 21% of patients learned their HIV result, completed their point-of-care CD4 count testing, and had their staging consultation all on the same day. The median time from enrolment to clinical staging for treatment decisions in this study dropped ten-fold from 32 days to 3 days. This is an important contribution to efforts worldwide to increase the efficiency and sustainability of antiretroviral therapy programmes. Improving clinic workflow, developing flexible staffing models to accommodate spikes in patients testing HIV-positive, and other innovations can increase the impact of point-of-care diagnostics on reducing loss-to-follow up, increasing treatment initiation, and ultimately improving patient survival.

5. Faith-based responses

Pentecostalism and AIDS treatment in Mozambique: creating new approaches to HIV prevention through anti-retroviral therapy


Pentecostal fervour has rapidly spread throughout central and southern Mozambique since the end of its protracted civil war in the early 1990s. In the peri-urban bairros and septic fringes of Mozambican cities African Independent Churches with Pentecostal roots and mainstream Pentecostals can now claim over half the population as adherents. Over this same period another important phenomenon has coincided with this church expansion: the AIDS epidemic. Pentecostalism and HIV have travelled along similar vectors and been propelled by deepening inequality. Recognising this relationship has important implications for HIV prevention and treatment strategies. The striking overlap between high HIV prevalence in peri-urban populations and high Pentecostal participation suggests that creative strategies, to include these movements in HIV programming, may influence the long-term success of HIV care and the scale-up of anti-retroviral treatment across the region. The provision of antiretroviral treatment has opened up new possibilities for engaging with local communities, especially Pentecostals and African Independent Churches, who are witnessing the immediate benefits of antiretroviral therapy. Expanded treatment may be the key to successful prevention as advocates of a comprehensive approach to the epidemic have long argued.


Editor’s note: At the end of Mozambique’s long civil war in the 1990s, people began to move more back and forth across the borders with South Africa and Zimbabwe. Among the things accompanying them were Pentecostal messages (more than half the population are now adherents) and HIV infection (HIV prevalence varies sharply by province but is higher in those adjacent to these countries). This interesting article analyses the impact of structural adjustment policies and class associations between different Christian religions in Mozambique on poverty and the response to HIV. It argues that Catholicism has a privileged position in health care delivery (the large majority of health care workers report that they are Catholics) and in interrelations with donors and foreign implementing partners. Pentecostals and African Independent Churches have excluded themselves or been excluded from HIV prevention programming based on their patriarchal theology, conservative social policy, and differences in moral discourse about sexual behaviour. Now the hope of antiretroviral therapy has opened up dialogue within Pentecostal churches, engendering a new social solidarity around AIDS, with members encouraged to learn their HIV status and seek treatment at public services. There is a tangible opportunity now for these large faith-based communities to break out of exclusion to participate actively as partners in public health treatment and prevention programming.
6. People living with HIV

Seroprevalence of HPV vaccine types 6, 11, 16 and 18 in HIV-infected women from South Africa, Brazil and Botswana


Many resource limited settings suffer from high rates of both cervical cancer and HIV. Limited HPV serology data are available from resource limited settings; such data could help describe local patterns of Human Papilloma Virus infection and predict vaccine efficacy. To determine seropositivity to HPV types 6, 11, 16 and 18 in HIV-infected women from South Africa, Botswana, and Brazil. HPV serotyping for high-risk types 6, 11, 16 and 18 was performed on samples collected from HIV-infected women from 2003-2010 using competitive Luminex Immuno Assay (HPV-4cLIA). Firnhaber and colleagues examined the association between seropositivity to these HPV types and country of enrollment, CD4, HIV-1 RNA level, and Pap smear. HPV serology results were available for 487 HIV-infected women (157, 170 and 160 from South Africa, Botswana, and Brazil respectively). Approximately 65% of women had serum antibodies to one of the 4 HPV types and less than 3% of women had antibodies to all 4 serotypes. Approximately 30% women demonstrated antibodies to type 16 HPV. Rates of seropositivity to HPV 11, and HPV 16+18 varied significantly between countries. Statistical difference was also shown in women in different age categories in the different countries. There was no difference in serology results compared by CD4 count, HIV viral load or Pap smear results. These data suggest that the quadrivalent vaccine may be effective in preventing HPV infection in these countries.


Editor's note: Cervical cancer is the third most common cancer in women with an estimated 85% of the global burden experienced in resource-constrained settings. Lack of access to services that provide early diagnosis of cervical abnormalities through visual screening with acetic acid or PAP tests means that HPV (human papilloma virus) infection that is persistent can develop undetected into cervical cancer. WHO reports that in 2007, 275,000 women died of cervical cancer, a cancer that can be cured if caught early and that is now vaccine-preventable. The two vaccines now available prevent cervical cancer from developing from HPV infection. As this article reveals, it is incorrect to assume that women living with HIV in countries as diverse as South Africa, Brazil, and Botswana have already had HPV infection. Only 3% of women had antibodies to all four of the types included in the quadrivalent vaccine, meaning that only they would not benefit from vaccination. Fully 35% had no evidence in their serum of previous HPV infection and 60% had no evidence of previous infection with the high-risk HPV subtypes 16 and 18. A number of trials are now underway assessing the safety and immunogenicity of HPV vaccination among women with HIV who have varying CD4 count levels and their results will inform policy and programming. In the meantime, preventing HPV infection in the first place through vaccination before sexual debut makes most sense for girls and now for boys worldwide.

7. Epidemiology

Molecular and epidemiological characterization of HIV-1 infection networks involving transmitted drug resistance mutations in Northern Greece


The objective of this study was to determine the contribution of transmission clusters to transmitted drug resistance in newly diagnosed antiretroviral-naive HIV-1-infected patients in Northern Greece during 2000-07. The prevalence of transmitted drug resistance was estimated in 369 individuals who were diagnosed with HIV-1 infection in the period 2000-07 at the National AIDS Reference Laboratory of Northern
Greece. Phylogenetic analysis was performed using a maximum likelihood method on partial pol sequences. Transmitted drug resistance was defined in accordance with the surveillance drug resistance mutation list (2009 update). The overall prevalence of transmitted drug resistance in the population studied was 12.5% [46/369, 95% confidence interval (CI) 9.1%-15.8%], comprising 7.6% (28/369) resistant to nucleoside reverse transcriptase inhibitors, 5.4% (20/369) resistant to non-nucleoside reverse transcriptase inhibitors and 3.3% (12/369) resistant to protease inhibitors. Dual class resistance was identified in 3.8% (14/369). Infection with subtype A was the sole predictor associated with transmitted drug resistance in multivariate analysis (odds ratio 2.15, 95% CI 1.10-4.19, P = 0.025). Phylogenetic analyses revealed three statistically robust transmission clusters involving drug-resistant strains, including one cluster of 12 patients, 10 of whom were infected with a strain carrying both T215 revertants and Y181C mutations. Skoura and colleagues' findings underline the substantial impact of transmission networks on transmitted drug resistance in Northern Greece.


Editor's note: HIV drug resistance can be transmitted and it can be acquired while on treatment. In both cases, it is a concern because it limits therapeutic options. Drug resistance testing at HIV diagnosis is routine in Greece and time trends in Northern Greece demonstrate a significant increase since 2000, particularly in resistance to NNRTIs (non-nucleoside reverse transcriptase inhibitors). Among the study overall population of people who were newly diagnosed and had never been on antiretroviral treatment, 53% of people were infected with subtype B, 33% with subtype A, and 14% with other subtypes. There was a strong correlation between sub-type A and transmitted drug resistance. In Northern Greece, patients with sub-type A belong predominantly to the native Greek population and are treated through the public health programme. Among the 17 people linked in clusters of cases with the same resistance patterns, 10 had dual drug resistant HIV-1 strains, highlighting not only the importance of surveillance at the population level but also of resistance testing to determine optimum treatment regimens for individuals who are starting their treatment pathway with a strike or even two against them.

8. Vaccines

Antibody-based protection against HIV infection by vectored immunoprophylaxis


Despite tremendous efforts, development of an effective vaccine against human immunodeficiency virus (HIV) has proved an elusive goal. Recently, however, numerous antibodies have been identified that are capable of neutralizing most circulating HIV strains. These antibodies all exhibit an unusually high level of somatic mutation 6, presumably owing to extensive affinity maturation over the course of continuous exposure to an evolving antigen. Although substantial effort has focused on the design of immunogens capable of eliciting antibodies de novo that would target similar epitopes 8–10, it remains uncertain whether a conventional vaccine will be able to elicit analogues of the existing broadly neutralizing antibodies. As an alternative to immunization, vector-mediated gene transfer could be used to engineer secretion of the existing broadly neutralizing antibodies into the circulation. Balazs and colleagues describe a practical implementation of this approach, which they call vectored immunoprophylaxis (VIP), which in mice induces lifelong expression of these monoclonal antibodies at high concentrations from a single intramuscular injection. This is achieved using a specialized adeno-associated virus vector optimized for the production of full-length antibody from muscle tissue. The authors show that humanized mice receiving VIP appear to be fully protected from HIV infection, even when challenged intravenously with very high doses of replication-competent virus. Their results suggest that successful translation of this approach to humans may produce effective prophylaxis against HIV.

Editor's note: Immunodeficiencies in humanized mice such as these NSG mice permit a wide range of primary human cells to be grafted without rejection. The mice lack mature T cells, B cells, and natural killer cells. They are deficient in multiple cytokine signaling pathways and have many defects in innate immunity. This makes them an excellent model for testing vaccines against HIV challenge. Following the recent identification of several neutralising antibodies (see HIV This Week issues 73 and 85), researchers have focused on how to make a vaccine that would generate these antibodies in humans. The approach described here, called vector immunoprophylaxis or VIP, has produced exciting results. The mice were grafted with human B cells and then adenovirus vectors expressing b12 or VRC01 were injected intramuscularly, with the mice being monitored for expression of antibodies over time. The mice were populated with human mononuclear cells and were then challenged intravenously with replication-competent HIV. Those that had generated high concentrations of antibody were protected from a challenge dose 100 times higher than necessary to infect the majority of animals. This VIP approach produced full-length antibodies identical in sequence to those produced by the human immune system. This approach could potentially be used for effective prophylaxis against any infectious disease for which broadly neutralising antibodies can be isolated but, in the first instance, the eye is on the prize of HIV.

9. Cost effectiveness

Cost-effectiveness of using HAART in prevention of mother-to-child transmission in the DREAM-project Malawi


Cost-effectiveness analysis is crucial in the management of the HIV epidemic, particularly in resource-limited settings. Such analyses have not been performed in the use of highly active antiretroviral therapy (HAART) for prevention of mother-to-child transmission (PMTCT). Orlando and colleagues conducted a cost-effectiveness analysis of HAART approach in Malawi for PMTCT. In 2 health centres in Malawi 6500 pregnant women were tested; 1118 pregnant women completed the entire Drug Resource Enhancement against AIDS and Malnutrition-Project Malawi (DREAM - PM) PMTCT protocol. The costs of the intervention were calculated using the ingredients method. Outcomes estimated were cost for infection averted and cost for DALY saved compared with no intervention. From a private perspective cost for HIV infection averted was US $998 and cost per DALY saved was US $35.36. From a public perspective, the result became negative as follows: -261 and -16.55, respectively (lower cost than the cost of the therapy for an HIV+ child). The univariate sensitivity analysis showed that the cost for DALY saved always remained under the threshold of US $50, largely under the threshold given by the per capita yearly income in Malawi (US $667 PPD). Administration of HAART in a PMTCT programme in resource-limited settings is cost-effective. Drugs and laboratory tests are the most significant costs, but further reduction of these expenses is possible.

prolongation of maternal life, reduction in stigma through improved quality of life, and declines in horizontal transmission to sexual partners. All PMTCT programmes should move as soon as possible to this option, and to Option B+, which sees women remain on antiretroviral therapy once they have started, through re-profiling of domestic funds and with international assistance.

Cost-effectiveness of early versus standard antiretroviral therapy in HIV-Infected adults in Haiti

In a randomized clinical trial of early versus standard antiretroviral therapy (ART) in HIV-infected adults with a CD4 cell count between 200 and 350 cells/mm(3) in Haiti, early ART decreased mortality by 75%. Koenig and colleagues assessed the cost-effectiveness of early versus standard ART in this trial. Trial data included use of ART and other medications, laboratory tests, outpatient visits, radiographic studies, procedures, and hospital services. Medication, laboratory, radiograph, labour, and overhead costs were from the study clinic, and hospital and procedure costs were from local providers. The authors evaluated cost per year of life saved, including patient and caregiver costs, with a median of 21 months and maximum of 36 months of follow-up, and with costs and life expectancy discounted at 3% per annum. Between 2005 and 2008, 816 participants were enrolled and followed for a median of 21 months. Mean total costs per patient during the trial were US$1,381 for early ART and US$1,033 for standard ART. After excluding research-related laboratory tests without clinical benefit, costs were US$1,158 (early ART) and US$979 (standard ART). Early ART patients had higher mean costs for ART (US$398 versus US$81) but lower costs for non-ART medications, CD4 cell counts, clinically indicated tests, and radiographs (US$275 versus US$384). The cost-effectiveness ratio after a maximum of 3 years for early versus standard ART was US$3,975/YLS (95% CI US$2,129/YLS-US$9,979/year of life saved) including research-related tests, and US$2,050/YLS excluding research-related tests (95% CI US$722/year of life saved-US$5,537/year of life saved). Initiating ART in HIV-infected adults with a CD4 cell count between 200 and 350 cells/mm(3) in Haiti, consistent with World Health Organization advice, was cost-effective (US$/YLS <3 times gross domestic product per capita) after a maximum of 3 years, after excluding research-related laboratory tests.


Editor's note: The World Health Organization changed it treatment guidelines in 2010 in part because of the findings of the CIPRA HT-001 trial in Haiti. The trial’s data safety and monitoring board (DSMB) had recommended stopping the trial early due to the substantial difference in mortality seen in those starting antiretroviral therapy when their CD4 count dropped to 350/μl compared to those who started at a CD4 count of 200/μl or less, the old WHO-recommended level. This study is the first to estimate cost-effectiveness of the new approach using trial data as opposed to simulation models. To do this fairly, all research-related costs had to be removed. The time horizon was short, limited by the 3–year length of the trial, which means that it is not possible to know whether the early group would continue to have a survival benefit over the long term once the later group starts on treatment or whether there will be differences in the need for more costly second line therapy. WHO designates health interventions as cost-effective if the cost per disability-adjusted life year (DALY) is less that 3 times a country’s gross domestic product (GDP) - Haiti's is 785 US$ - or under a threshold per life year saved – Haiti’s in 2009 was 2355 US$. This study shows that early initiation of antiretroviral therapy is cost-effective for Haiti. Decision-makers in other countries facing budget constraints should consider economic analyses as a helpful element in setting priorities. Access to treatment and support for retention in care should ensured first for the sickest patients but expansion of treatment eligibility to get more people on treatment earlier in their HIV disease course should be the next step.
The negative effects of stigma on persons living with HIV (PLHIV) have been documented in many settings and it is thought that stigma against PLHIV leads to more difficulties for those who need to access HIV testing, treatment and care, as well as to limited community uptake of HIV prevention and testing messages. In order to understand and prevent stigma towards PLHIV, it is important to be able to measure stigma within communities and to understand which factors are associated with higher stigma. To analyze patterns of community stigma and determinants to stigma toward PLHIV, Pharris and colleagues performed an exploratory population-based survey with 1874 randomly sampled adults within a demographic surveillance site (DSS) in rural Vietnam. Participants were interviewed regarding knowledge of HIV and attitudes towards persons living with HIV. Data were linked to socioeconomic and migration data from the DSS and latent class analysis and multinomial logistic regression were conducted to examine stigma group sub-types and factors associated with stigma group membership. They found unexpectedly high and complex patterns of stigma against PLHIV in this rural setting. Women had the greatest odds of belong to the highest stigma group (OR 1.84, 95% CI 1.42-2.37), while those with more education had lower odds of highest stigma group membership (OR 0.45, 95% CI 0.32-0.62 for secondary education; OR 0.19, 95% CI 0.10-0.35 for tertiary education). Long-term migration out of the district (OR 0.61, 95% CI 0.4-0.91), feeling at-risk for HIV (OR 0.42, 95% CI 0.27-0.66), having heard of HIV from more sources (OR 0.44, 95% CI 0.3-0.66), and knowing someone with HIV (OR 0.76, 95% CI 0.58-0.99) were all associated with lower odds of highest stigma group membership. Nearly 20% of the population was highly unsure of their attitudes towards PLHIV and persons in this group had significantly lower odds of feeling at-risk for HIV (OR 0.54, 95% CI 0.33-0.90) or of knowing someone with HIV (OR 0.32, 95% CI 0.22-0.46). Stigma towards PLHIV is high generally, and very high in some sub-groups, in this community setting. Future stigma prevention efforts could be enhanced by analysing community stigma sub-groups and tailoring intervention messages to community patterns of stigma.


Editor’s note: In 2006, Vietnam strengthened legislation and extended protection for people living with HIV by prohibiting HIV-related stigma and discrimination and by promoting their rights to confidentiality, medical care, and community integration. Despite this existing legal framework and a focus on stigma reduction in government education programmes, this study in a rural population found high levels of stigma and identified three classes of people: less stigmatising, ambivalent, and highly stigmatising, using a latent class analysis approach. This approach, which has been used to tailor marketing campaigns to specific segments of the population, grouped people according to their responses to 8 HIV-related stigma statements. The statements themselves were based on the stigma concepts of labelling, stereotyping, separation, status loss, and discrimination. Those with the most stigmatising attitudes were less likely to know someone with HIV, did not judge themselves to be at risk, and had heard of HIV from fewer sources. In a society in which many perceive HIV to be associated with social evils, putting a human face on HIV would be one approach that could help reduce stigma. More broadly, analysis of community patterns of stigma using latent class analysis can inform effective programming, focused on reducing the stigma that influences people not to come forward to learn their HIV serostatus and that undermines adherence to treatment and access to social support for those who know they are living with HIV.
Initial validation of the HIV/AIDS Provider Stigma Inventory (HAPSI), piloted on a sample of 174 nursing students, supported the psychometric qualities of a suite of measures capturing tendencies to stigmatize and discriminate against people living with HIV (PLHIV). Derived from social psychology and mindfulness theories, separate scales addressing awareness, acceptance, and action were designed to include notions of labelling, stereotyping, outgrouping, and discriminating. These were enhanced to capture differences associated with personal characteristics of PLHIV that trigger secondary stigma (e.g., sexual orientation, injection drug use, multiple sex partners) and fears regarding instrumental and symbolic stigma. Reliabilities were strong (coefficients $\alpha$ for 16 of 19 resulting measures ranged from 0.80 to 0.98) and confirmatory factor analyses indicated good model fit for two multidimensional (Awareness and Acceptance) and one unidimensional (Action) measure. Evidence of convergent construct validity supported accuracy of primary constructs. Implications for training and professional socialization in health care are discussed.


Editor's note: Current concepts of HIV-related stigma often categorise stigma as instrumental stigma (fear of physical contagion), symbolic stigma (morality- or values-based judgement), felt, perceived, or internalised stigma (experiences of prejudice and discrimination), courtesy stigma (felt by health care providers caring for people living with HIV or by their families), and enacted stigma (discriminatory actions). Research on the measurement of stigma has focused primarily on the general public and the lived experiences of people living with HIV, with only a few studies having developed scales to assess stigma in health care settings. These researchers developed an instrument that assists providers in assessing their own awareness of negative attitudes, in accepting that there are potential consequences to carrying these views into interactions with patients living with HIV, and in acting intentionally to prevent their prejudice from provoking enacted discrimination. It uses a mindfulness approach, drawn from ancient philosophical traditions of Asia, to promote thoughtful rather than automatic reactions through reflection about troubling situations and their meaning. This tool, once further validated, could be used during training or in continuing education as part of professional socialisation focused on interpersonal skills.

11. Discordant couples

Outside sexual partnerships and risk of HIV acquisition for HIV uninfected partners in African HIV serodiscordant partnerships


As African countries scale up couples HIV testing, little is known about sexual behaviours and HIV risk for HIV-uninfected partners in known HIV serodiscordant relationships. Ndase and colleagues conducted a prospective study of 3,380 HIV serodiscordant partnerships from 7 African countries. Self-reported sexual behaviour data were collected quarterly from HIV-uninfected partners. The proportion of HIV-uninfected partners reporting sex with their known primary HIV infected partner decreased during follow-up (from 93.5% in the prior month at baseline to 73.2% at 24 months, $p<0.001$). Simultaneously, an increasing proportion reported sex with an outside partner (from 3.1% to 13.9%, $p<0.001$). A small proportion (<5%, stable throughout follow-up) reported sex with the infected partner and an outside partner in the same month (concurrent). Unprotected sex was more common with outside partners than with their primary known HIV infected partners (risk ratio 4.6; 95% CI 4.2-5.2). HIV incidence was similar for those reporting sex only with their primary HIV-infected partner compared to those who reported an outside partner (2.87 vs. 3.02 per 100 person-years, $p=0.7$), although those who had outside partners were more likely to acquire HIV that was virologically distinct from that of their primary partner ($p<0.001$). For uninfected members of HIV-serodiscordant couples, sex with the infected partner declined as sex with outside
partners increased, likely reflecting relationship dissolution and risk shifting from a known infected partner. Risk reduction messages for HIV uninfected partners in serodiscordant partnerships should include strategies to reduce HIV acquisition from outside partners.


**Editor's note:** HIV-negative people in serodiscordant partnerships rarely have contact with health care providers after receiving their initial HIV-negative test result. As well, little is known about the evolution of sexual practices in serodiscordant couples after they learn their serostatus. This study, analysing data from a herpes suppression trial (the HIV-positive partner also had herpes simplex virus-2 infection) provides useful information about sexual practices both within and outside the couple over time. Sex within couples declined for both men (94% to 73%) and women (92% to 74%) during the 2 years after they learned their results and sex with an outside partner increased for both men (4% to 19%) and women (0.5% to 4%). Of note, when an outside partner was reported by the HIV-negative partner in a quarterly interview there was little concurrency—less than 5% reported sex both within and outside the couple in the previous month. There was a steady increase over time for both men and women in the proportions reporting no sexual activity and reporting sexual activity only with outside partners. The most striking finding is low reported condom use with outside partners, reflecting risk perceptions that may not mirror true risk. Of the 21 people reporting outside partners who seroconverted, 18 acquired HIV outside the partnership while of the 130 reporting no outside partners who seroconverted, 105 of these infections could be biologically linked to the seropositive partner. As the scaling up of HIV testing and counselling proceeds, more serodiscordant couples will learn their status—an estimated 50% of people living with HIV in sub-Saharan Africa have a partner who is not infected. Tailored counselling for these couples can help them support each other to better perceive their HIV transmission and acquisition risks to protect themselves and others.

12. Civil society responses

**HIV-prevention interventions targeting men having sex with men in Africa: field experiences from Cameroon**


The HIV prevalence rate among men who have sex with men in Africa is high, yet a limited number of prevention interventions target this vulnerable group. The study aims to explore factors affecting the design and implementation of HIV-prevention interventions for men who have sex with men in Cameroon using Alternatives-Cameroun as a case study. It further examines the context in which these interventions are created and implemented. **Operating in a repressive environment, facing criminalisation and stigmatisation, one organisation, Alternatives-Cameroun, has adopted an 'umbrella approach', using human rights as a platform from which to negotiate for greater recognition of men who have sex with men.** Success has been achieved through a *proximity approach to prevention*, setting up a local Access Centre and using a base of volunteers to create interventions that venture into the community. The organisation faces many obstacles such as repressive legislation, stigmatisation, and volunteer fatigue. Findings reveal that understanding local realities and reinforcing multi-sectoral mobilisation around men who have sex with men issues are important first steps towards launching HIV-prevention interventions for men who have sex with men in sub-Saharan Africa.


**Editor's note:** Alternatives-Cameroun was launched in 2006 in Douala to serve primarily men who have sex with men (locally called *nkouandengué*) in an environment of denial, stigmatisation, and criminalisation that is not uncommon in other parts of Africa. This case study reveals that the widespread heterocentric perception of HIV in Cameroon influences the risk perception of men who have sex with men. Beliefs that anal sex cannot transmit HIV, a male partner is less risky for a man because there is no risk of pregnancy,
and condoms are only for contraception are not uncommon among the men being reached by this community-based organisation. Men may try to camouflage their sexual orientation by having a girlfriend or by having multiple male partners so that they are not seen too often with the same man, which would arouse suspicion. Article 347bis of the Cameroon Penal Code, which criminalises homosexuality with a punishment of imprisonment from 6 months to 5 years and a fine of from 20,000 to 200,000 francs CFA, has created a climate of fear and repression reinforcing social marginalisation and constricting the methods that Alternatives-Cameroun can use to reach men who have sex with men. Based on ‘proximity approach’ principles, it conducts outreach to venues (both bars/clubs and virtual electronic networks), conducts educational workshops, refers men to gay-friendly physicians, and trains peer leaders to reach out to hidden men. The focus is on sexual practices and risk behaviours rather than on sexual orientation or identity. Although the experiences and sociolegal constraints of Alternatives-Cameroun are context-specific, they have resonance for countries across Africa that have not yet repealed similar repressive laws that contravene human rights principles.

13. Male circumcision devices

Safety and efficacy of the PrePex™ Device for rapid scale up of male circumcision for HIV prevention in resource-limited settings


Bitega and colleagues assessed the safety and efficacy of the PrePex device for nonsurgical circumcision in adult males, as part of a comprehensive HIV prevention program in Rwanda. They conducted a single-centre 6-week non-controlled study in which healthy men underwent circumcision using the PrePex device, which employs fitted rings to clamp the foreskin, leading to distal necrosis. In the first phase of the study, the feasibility of the procedure was tested on 5 subjects in a sterile environment; in the main phase, an additional 50 subjects were circumcised in a non-sterile setting, by physicians or a nurse. Outcome measures included the rate of successful circumcision, time to complete healing, pain, and adverse events. In the feasibility phase, all 5 subjects achieved complete circumcision without adverse events. In the main phase, all 50 subjects achieved circumcision with 1 case of diffuse edema following device removal, which resolved with minimal intervention. Pain was minimal except briefly during device removal (day 7 after placement in most cases). The entire procedure was bloodless, requiring no anaesthesia, no suturing, and no sterile settings. Subjects had no sick/absent days associated with the procedure. Median time for complete healing was 21 days after device removal. There were no instances of erroneous placement and no mechanical problems with the device. The PrePex device was safe and effective for nonsurgical adult male circumcision without anaesthesia or sterile settings, and may be useful in mass circumcision programs to reduce the risk of HIV infection, particularly in resource-limited settings.


Editor’s note: As noted in the Editor’s notes on the Shang Ring in HIV This Week Issue 92, WHO and UNAIDS recommend three surgical techniques for adult male circumcision: the forceps guided method, the sleeve resection method, and the dorsal slit method (http://www.malecircumcision.org). In the absence of task sharing and other methods to optimise the volume and efficiency of male circumcision service delivery, these methods entail 20 to 30 minutes of surgical time. Given the millions of adult male circumcisions that countries are aiming to achieve by 2015, there is tremendous interest in the potential time-saving features of medical devices. The PrePex™ device has many advantages: no need for injected anaesthesia, no sutures, no crushing or cutting of live foreskin, and a short procedure time of about 5 minutes for placement and removal 7 days later. This is a slow compression device that compresses the foreskin, cutting off circulation distally. The Rwanda team reported results at ICASA in December on their field trial of 590 nurse-administered PrePex™ male circumcisions with good results on safety and effectiveness. The PrePex™
The safety profile and acceptability of a disposable male circumcision device in Kenyan men undergoing voluntary medical male circumcision


Musau and colleagues set out to establish the safety and effectiveness as well as the acceptability of the Alisklamp® device for male circumcision among Kenyan men. To qualify for this hospital based, prospective, interventional cohort study one needed to be an uncircumcised adult male who was HIV-negative with no comorbid factors or genitourinary anomalies precluding circumcision. A total of 58 men were recruited from a population of 90. Outcome measures were the safety profile of Alisklamp® and its efficiency and acceptability by participants. All 58 procedures were completed without device malfunction, haemorrhage or undesirable preputial excision. Mean ± SD procedure time was 2.43 ± 1.36 minutes and mean device removal time was 15.8 ± 7.4 seconds. There were 2 adverse events, including mild edema and superficial wound infection related to poor hygiene in 1 case each. All men resumed routine activity immediately after circumcision. Of the 58 participants 25.9% experienced mild nocturnal erectile pains that required no medication. During 6-week follow-up all men were satisfied with the procedure, tolerated the device well, and would recommend it to a friend. Alisklamp® has an excellent safety profile and excellent acceptability among men who undergo circumcision using the device. This technique is easy to teach and it would prove to be a handy device to scale up the rate of male circumcision. Based on these findings the device merits a comparative clinical trial.


Editor’s note: Male circumcision surgical devices have the potential to improve the cost-effectiveness of male circumcision, although referral to a standard surgical set-up will be needed for some men for whom a device will not be appropriate. This is the first study of use of the Alisklamp® device for male circumcision of adult men in sub-Saharan Africa and the results are promising. Although local anaesthesia is required for device placement, the average procedure time was about 2.5 minutes for placement and 16 seconds for removal. The next steps for this device will be a clinical trial and a field trial, after which it can be evaluated by the WHO Technical Advisory Group on Innovations in Male Circumcision that has a mandate to examine data on new circumcision devices formally submitted to it. Although over 1.3 million medical male circumcisions have been performed since the 2007 WHO/UNAIDS recommendations, an estimated 19 million remain to be completed by 2015. There is no doubt that, when approved, medical devices for male circumcision can help accelerate the scale-up.

14. National responses

Calculation of direct antiretroviral treatment costs and potential cost savings by using generics in the German HIV ClinSurv cohort


The study aimed to determine the cost impact of antiretroviral drugs by analysing a long-term follow-up of direct costs for combined antiretroviral therapy regimens in the nationwide long-term observational multi-centre German HIV ClinSurv Cohort. The second aim was to develop potential cost saving strategies by modelling different treatment scenarios. Antiretroviral regimens from 10,190 HIV-infected patients from 11 participating ClinSurv study centres have been investigated since 1996. Biannual data on antiretroviral
therapy initiation, antiretroviral therapy changes, surrogate markers, clinical events, and the Centre of Disease Control (CDC) stage of HIV disease are reported. Treatment duration was calculated on a daily basis via the documented dates for the beginning and end of each antiretroviral drug treatment. Prices were calculated for each individual regimen based on actual office sales prices of the branded pharmaceuticals distributed by the license holder including German taxes. During the 13-year follow-up period, 21,387,427 treatment days were covered. Cumulative direct costs for antiretroviral drugs of €812,877,356 were determined according to an average of €42.08 per day (€7.52 to €217.70). Since cART is widely used in Germany, the costs for an entire regimen increased by 13.5%. Regimens are more expensive in the advanced stages of HIV disease. The potential for cost savings was calculated using non-nucleotide-reverse-transcriptase-inhibitor, NNRTI, more frequently instead of ritonavir-boosted protease inhibitor, PI/r, in first line therapy. This calculation revealed cumulative savings of 10.9% to 19.8% of daily treatment costs (50% and 90% substitution of PI/r, respectively). Substituting certain branded drugs by generic drugs showed potential cost savings of between 1.6% and 31.8%. Analysis of the data of this nationwide study reflects disease-specific health services research and will give insights into the cost impacts of antiretroviral therapy, and might allow a more rational allocation of resources within the German health care system.


Editor's note: Using this huge data set, compiled since January 1999 and comprised of over 21 million antiretroviral treatment days, this study assessed trends in prescribing patterns and in the direct costs of various antiretroviral regimens to the German health care system. Among the interesting findings are the lower direct drug costs for women than for men because women in Germany tend to present earlier in their disease course, the historical evidence of treatment interruptions in 2003-2004 (12.1% per year) declining to 6.3% in 2008, and the large number of different drug regimens (197), although the top 10 account for 90% of treatment regimens. Colour graphs show the cumulative use of antiretroviral classes by year and mean daily treatment costs by class and by year, adjusting for the German consumer price index. With several drugs having come off patent or soon to do so, the authors calculate the cost savings that generic formulations could make at a time when German, European, and USA treatment guidelines recommend starting antiretroviral therapy at 500 CD/μl with 2 NRTI and a third drug which can be an NNRTI or a ritonavir-boosted protease inhibitor or an integrase inhibitor. This database of over 10,000 patients has the potential to provide the answers for national decision-making in Germany, whose health care system operates on an economic efficiency principle, on how best to allocate resources.
That was *HIV this week*, signing off.

**Editors' notes on journal access**

**For readers in all countries:**

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