

HIV This Week: what scientific journals said

Welcome to the sixtieth issue of *HIV This Week*! In this issue, we cover **men who have sex with men** (increasingly virtual gay communities must mean new HIV prevention strategies; is there a role for gay community in HIV prevention today?; rationale for a trial of male circumcision in men who have sex with men), **country responses** (human rights considerations in country strategic plans for universal access: glass half full or half empty?), **stigma** (fighting back: a conceptual framework for a multifaceted, multilevel strategy; Iranian high school girls have much to learn about people living with HIV), **behaviour change** (promising results from the Stepping Stones cluster randomised controlled trial in South Africa; effectiveness of skills building for sexual risk reduction in a trial among women in substance abuse treatment programs in the US), **biomedical HIV prevention trials** (why adherence in randomised controlled trials is so important; sexual risk behaviour in trials: does it improve or get worse?), **treatment adherence** (food supplementation improves adherence in Lusaka, Zambia; memory aids and social support are predictors of adherence in Southwest Ethiopia), **diagnostics** (data from South Africa call into question WHO clinical and CD4 count criteria for antiretroviral treatment failure; temperature stability of HIV RNA in plasma specimens), **basic science** (evidence from a paleovirological investigation reveals that HIV may have crossed to humans early in the 20th century; lessons to be learned when an AIDS patient and an elite suppressor handle the same virus differently), **surveillance** (how good and how bad is 'know your epidemic' in low- and middle-income countries; what do population-based surveys in sub-Saharan Africa contribute to HIV surveillance), **women's health** (two-thirds of women living with HIV may have high risk human papillomavirus infections; women have better prognosis than men in an analysis of 23 seroconverter studies in high-income countries), and **cultural determinants of risk** (will sexual cleansing rituals in Western Kenya follow the road of other changes?).

To find out how you can access a majority of scientific journals free of charge, please see the last page of this issue or check the *HIV This Week* website at <http://hivthisweek.unaids.org>

We want to be as helpful to you as we can, so please let us know what your interests are and what you think of *HIV This Week* by sending a comment to hivthisweek@unaids.org or by posting one on the *HIV This Week* website. If you would like to recommend an article for inclusion in *HIV This Week* or if you no longer wish to receive *HIV This Week* pdf issues by email, please contact us at hivthisweek@unaids.org. Don't forget that you can find a wealth of information on the HIV epidemic and responses to it at www.unaids.org

Cate Hankins
Chief Scientific Adviser

Nicolai Lohse
Research Officer

Tania Lemay
Research Consultant

1. *Men who have sex with men*

Simon Rosser BR, West W, Weinmeyer R. Are gay communities dying or just in transition? Results from an international consultation examining possible structural change in gay communities. *AIDS Care*. 2008 May;20(5):588-95.

This study sought to identify how urban gay communities are undergoing structural change, reasons for that change, and implications for HIV prevention planning. Key informants (N=29) at the AIDS Impact Conference from 17 cities in 14 countries completed surveys and participated in a facilitated structured dialog about whether gay communities are changing, and if so, how they are changing. In all cities, the virtual gay community was identified as currently larger than the offline physical community. Most cities identified that while the gay population in their cities appeared stable or growing, the gay community appeared in decline. Measures included greater integration of heterosexuals into historically gay-identified neighbourhoods and movement of gay persons into suburbs, decreased number of gay bars/clubs, less attendance at gay events, less volunteerism in gay or HIV/AIDS organizations, and the overall declining visibility of gay communities. Participants attributed structural change to multiple factors including gay neighbourhood gentrification, achievement of civil rights, less discrimination, a vibrant virtual community, and changes in drug use. Consistent with social assimilation, gay infrastructure, visibility, and community identification appears to be decreasing across cities. HIV prevention planning, interventions, treatment services, and policies need to be re-conceptualized for men who have sex with men in the future. Four recommendations for future HIV prevention and research are detailed.

Editors' note: Applying an ecological model of health behaviour (intra-individual, interpersonal, institutional/organisational, community, structural) to understanding the resurgent HIV epidemic among gay men living primarily in the global north reveals that many ingredients of successful early HIV prevention (community activism, community-appropriate interventions, and a sense of solidarity against the virus) are ill adapted to current realities of increasingly virtual gay communities. Structural changes in gay communities have reduced the effectiveness of HIV prevention making it high time to take stock, rethink, and tailor effective strategies to reduce HIV incidence among men who have sex with men.

Rowe MS, Dowsett GW. Sex, love, friendship, belonging and place: Is there a role for 'Gay Community' in HIV prevention today? *Cult Health Sex*. 2008 May; 10(4):329-44.

The decade since highly active anti-retroviral therapy arrived has been a time of change for gay men in the West. HIV incidence rates have been levelling off-and in some cities, increasing markedly-for the first time since the early years of the pandemic. New sexual subcultures have found expression, including Internet chat rooms, 'poz-only' sex parties, 'barebacking' and crystal methamphetamine use. These circumstances force a re-evaluation of HIV prevention targeting gay communities. Rowe and Dowsett examine the antecedents of current HIV-prevention dilemmas in findings from a qualitative study of gay men who were personally and professionally engaged in HIV in Sydney, Australia, in 1997-1998, immediately after the 'protease moment'. The men's lives were characterized by constant and difficult negotiation of gay subjectivities. They did not find a place of uniform belonging in the gay community; rather, ambivalence-toward the gay community and HIV prevention-and fragmentation emerged as themes. The authors' findings suggest that by the late 1990s, the ethos of safe sex developed in the early HIV period was no longer a unifying cultural value.

They explore the conditions that led to this shift and the implications for HIV prevention in the 21st century. **Editors' note: These Australian findings from 1997-98 suggest that the advent of effective combination treatment constituted a turning point in gay history from which the logic of the safe sex culture as a unifying and enduring cultural value began to falter. With potential resonance for HIV prevention programmes elsewhere, this underscores the need to recognise that much of what gay men experience as gay community lies outside what are traditionally understood to be a community's geographic, social, and conceptual boundaries.**

Millett GA, Flores SA, Marks G, Reed JB, Herbst JH. Circumcision status and risk of HIV and sexually transmitted infections among men who have sex with men: a meta-analysis. *JAMA*. 2008 Oct 8;300(14):1674-84.

Randomized controlled trials and meta-analyses have demonstrated that male circumcision reduces men's risk of contracting human immunodeficiency virus (HIV) infection during heterosexual intercourse. Less is known about whether male circumcision provides protection against HIV infection among men who have sex with men. Millett et al set out to quantitatively summarize the strength of the association between male circumcision and HIV infection and other sexually transmitted infections (STIs) across observational studies of men who have sex with men. They undertake a comprehensive search of databases, including MEDLINE, EMBASE, ERIC, Sociofile, PsycINFO, Web of Science, and Google Scholar, and correspondence with researchers, to find published articles, conference proceedings, and unpublished reports through February 2008. Of 18 studies that quantitatively examined the association between male circumcision and HIV sexually transmitted infection among men who have sex with men, 15 (83%) met the selection criteria for the meta-analysis. Independent abstraction was conducted by pairs of reviewers using a standardized abstraction form. Study quality was assessed using the Newcastle-Ottawa Scale. A total of 53,567 men who have sex with men (52% circumcised) were included in the meta-analysis. The odds of being HIV-positive were nonsignificantly lower among men who have sex with men who were circumcised than uncircumcised (odds ratio, 0.86; 95% confidence interval, 0.65-1.13; number of independent effect sizes [k] = 15). Higher study quality was associated with a reduced odds of HIV infection among circumcised men who have sex with men (beta, -0.415; P = .01). Among men who have sex with men who primarily engaged in insertive anal sex, the association between male circumcision and HIV was protective but not statistically significant (odds ratio, 0.71; 95% confidence interval, 0.23-2.22; k = 4). Male circumcision had a protective association with HIV in studies of men who have sex with men conducted before the introduction of highly active antiretroviral therapy (odds ratio, 0.47; 95% confidence interval, 0.32-0.69; k = 3). Neither the association between male circumcision and other sexually transmitted infections (odds ratio, 1.02; 95% confidence interval, 0.83-1.26; k = 8), nor its relationship with study quality was statistically significant (beta, 0.265; P = .47). The authors conclude that pooled analyses of available observational studies of men who have sex with men revealed insufficient evidence that male circumcision protects against HIV infection or other sexually transmitted infections. However, the comparable protective effect of male circumcision in men who have sex with men studies of men who have sex with men conducted before the era of highly active antiretroviral therapy, as in the recent male circumcision trials of heterosexual African men, supports further investigation of male circumcision for HIV prevention among men who have sex with men. **Editors' note: The observational data on HIV risk and circumcision status among men who have sex with**

men, even those who primarily engage in insertive sex, do not suggest the strong protective effect seen for men who have sex with women. In fact, the findings are at best a non-significant trend and at worse a chance finding. However, male circumcision was significantly protective for men having sex with men before the advent of antiretroviral treatment. The feasibility of a randomised controlled clinical trial to resolve the question of whether male circumcision confers a significant level of partial protection to men who have sex with men in the era of antiretroviral treatment is being assessed in Peru where overenrolment of primarily insertive men would increase the statistical power of a trial.

2. Country responses

Gruskin S, Tarantola D. Universal Access to HIV prevention, treatment and care: assessing the inclusion of human rights in international and national strategic plans. *AIDS*. 2008 Aug;22 Suppl 2:S123-32.

Rhetorical acknowledgment of the value of human rights for the AIDS response continues, yet practical application of human rights principles to national efforts appears to be increasingly deficient. We assess the ways in which international and national strategic plans and other core documents take into account the commitments made by countries to uphold human rights in their efforts towards achieving Universal Access. Key documents from the Joint United Nations Programme on HIV and AIDS (UNAIDS), the World Health Organization (WHO), the World Bank, the Global Fund to Fight AIDS, TB and Malaria (GFATM) and the US President's Emergency Plan for AIDS Relief (PEPFAR) were reviewed along with 14 national HIV strategic plans chosen for their illustration of the diversity of HIV epidemic patterns, levels of income and geographical location. Whereas human rights concepts overwhelmingly appeared in both international and national strategic documents, their translation into actionable terms or monitoring frameworks was weak, unspecific or absent. Future work should analyse strategic plans, plans of operation, budgets and actual implementation so that full advantage can be taken, not only of the moral and legal value of human rights, but also their instrumental value for achieving Universal Access. **Editors' note: This review is a mini-primer on human rights, presenting definitions of key human rights terms relevant to universal access, including 'duty bearers', rights holders', and the 3AQ (availability, accessibility, acceptability and quality). It finds that in most countries assessed, universal access remains primarily equated with treatment, underscoring the need to emphasise prevention as the mainstay of universal access. As well, law reform, ensuring confidentiality protection, preventing violence against women, and other strategies beyond traditional health sector approaches essential to an effective response receive little attention. Important strides have been made in the recognition of marginalised communities but much more is needed to operationalise human rights in national HIV strategic plans.**

3. Stigma

Mahajan AP, Sayles JN, Patel VA, Remien RH, Sawires SR, Ortiz DJ, Szekeres G, Coates TJ. Stigma in the HIV/AIDS epidemic: a review of the literature and recommendations for the way forward. *AIDS*. 2008 Aug;22 Suppl 2:S67-79.

Although stigma is considered a major barrier to effective responses to the AIDS epidemic, stigma reduction efforts are relegated to the bottom of AIDS programme priorities. The complexity of HIV-related stigma is often cited as a primary reason for the limited response

to this pervasive phenomenon. In this paper, Mahajan et al systematically review the scientific literature on HIV-related stigma to document the current state of research, identify gaps in the available evidence and highlight promising strategies to address stigma. They focus on the following key challenges: defining, measuring and reducing HIV-related stigma as well as assessing the impact of stigma on the effectiveness of HIV prevention and treatment programmes. Based on the literature, the authors conclude by offering a set of recommendations that may represent important next steps in a multifaceted response to stigma in the AIDS epidemic. **Editors' note: Stigma may be defined as a mark of disgrace, an attribute that is deeply discrediting, or a difference that taints and discounts a person. The conceptual framework presented here starts with the foundation of inequalities in social, political, and economic power that promulgate labelling, stereotyping, separation/status loss, and discrimination. Moving toward consensus on how best to define, measure, and diminish stigma is the first step. One component would be community organising among people living with HIV and their sympathetic supporters to 'unleash the power of resistance on the part of the stigmatised' but stigma will only be effectively reduced through an overarching multifaceted, multilevel approach.**

Ghabili K, Shoja MM, Kamran P. The Iranian female high school students' attitude towards people with HIV/AIDS: a cross-sectional study. *AIDS Res Ther.* 2008 Jul 22;5:15.

Acquired Immunodeficiency Syndrome (AIDS) has become an important public health hazard in Iran. It is believed that AIDS-related knowledge does not necessarily translate into behaviour modification. Hence, it has been suggested that culturally appropriate educational campaigns should be implemented to obtain satisfactory outcomes. Here, Ghabili et al evaluated the female high school students' attitude towards HIV in Tabriz, Iran to assess the cultural needs for the related educational programs and to discover sources of information about AIDS. Anonymous, self-administered questionnaires were filled by the young female students. Among 300 students, 91% agreed that being an HIV carrier should not be an obstacle to obtaining education and employment. Moreover, 72.5% of the students declared that the community should be informed of HIV-positive people. In addition, one-tenth declared that they would feel extremely uncomfortable towards their HIV infected classmate. In addition, only 16% of the students stated that they would continue to shop at HIV infected grocer's store. The mass media and the experts were the major source and the most reliable source of information about AIDS, respectively. Tabrizian female students have overall negative attitudes towards HIV. HIV-related educational campaigns should target the students, society, and the families with emphasizing the leading roles of health staff. **Editors' note: Among the striking negative attitudes among Iranian high school girls are the views that children who are HIV carriers should be send to special schools/classes (41%), special hospitals should be created for AIDS patients (86%), and most AIDS patients do not care if they infect other people too (66%). Clearly, school-based education programmes need to anchored in society-wide educational campaigns, using credible information and spokespeople to create new community and family understandings about HIV.**

4. Behaviour change

Jewkes R, Nduna M, Levin J, Jama N, Dunkle K, Puren A, Duvvury N. Impact of Stepping Stones on incidence of HIV and HSV-2 and sexual behaviour in rural South Africa: Cluster randomised controlled trial. *BMJ*. 2008 Aug 7;337:a506. doi: 10.1136/bmj.a506

Jewkes et al aimed to assess the impact of Stepping Stones, a HIV prevention programme, on incidence of HIV and herpes simplex type 2 (HSV-2) and sexual behaviour. Cluster randomised controlled trial was conducted in 70 villages (clusters) in the Eastern Cape province of South Africa. Participants were 1360 men and 1416 women aged 15-26 years, who were mostly attending schools. Stepping Stones, a 50 hour programme, aims to improve sexual health by using participatory learning approaches to build knowledge, risk awareness, and communication skills and to stimulate critical reflection. Villages were randomised to receive either this or a three hour intervention on HIV and safer sex. Interviewers administered questionnaires at baseline and 12 and 24 months and blood was tested for HIV and HSV-2. The primary outcome measure was HIV incidence. Other outcomes being incidence of HSV-2, unwanted pregnancy, reported sexual practices, depression, and substance misuse. The authors found that there was no evidence that Stepping Stones lowered the incidence of HIV (adjusted incidence rate ratio 0.95, 95% confidence interval 0.67 to 1.35). The programme was associated with a reduction of about 33% in the incidence of HSV-2 (0.67, 0.46 to 0.97; P=0.036)-that is, Stepping Stones reduced the number of new HSV-2 infections over a two year period by 34.9 (1.6 to 68.2) per 1000 people exposed.

Stepping Stones significantly improved a number of reported risk behaviours in men, with a lower proportion of men reporting perpetration of intimate partner violence across two years of follow-up and less transactional sex and problem drinking at 12 months. In women desired behaviour changes were not reported and those in the Stepping Stones programme reported more transactional sex at 12 months. The authors concluded that Stepping Stones did not reduce incidence of HIV but had an impact on several risk factors for HIV-notably, HSV-2 and perpetration of intimate partner violence. TRIAL REGISTRATION: Clinical Trials NCT00332878. **Editors' note: Stepping Stones is a participatory HIV prevention programme that aims to be gender transformative, improving sexual health through building stronger, more gender equitable relationships. Developed for use in Uganda in 1995, it has been adapted for 17 settings, used in over 40 countries, translated into 13 languages, used with hundreds of thousands of individuals, but never has been evaluated using a randomised controlled trial design with biological outcomes. Although no impact on HIV was found, possibly due to sample size limitations, the reduced incidence of herpes simplex type 2 is significant and although women did not show much behaviour change, men reported significant behaviour change that likely reflects changing ideas of masculinity.**

Tross S, Campbell AN, Cohen LR, Calsyn D, Pavlicova M, Miele GM, Hu MC, Haynes L, Nugent N, Gan W, Hatch-Maillette M, Mandler R, McLaughlin P, El-Bassel N, Crits-Christoph P, Nunes EV. Effectiveness of HIV/STD sexual risk reduction groups for women in substance abuse treatment programs: results of NIDA Clinical Trials Network Trial. *J Acquir Immune Defic Syndr*. 2008 Aug 15;48(5):581-9.

Because drug-involved women are among the fastest growing groups with AIDS, sexual risk reduction intervention for them is a public health imperative. The objective was to test effectiveness of HIV/STD safer sex skills building (SSB) groups for women in community drug treatment. This was a randomized trial of SSB versus standard HIV/STD Education (HE); assessments at baseline, 3 and 6 months. The participants were women recruited from

12 methadone or psychosocial treatment programs in Clinical Trials Network of National Institute on Drug Abuse. Five hundred fifteen women with ≥ 1 unprotected vaginal or anal sex occasion (USO) with a male partner in the past 6 months were randomized. In SSB, five 90-minute groups used problem solving and skills rehearsal to increase HIV/STD risk awareness, condom use, and partner negotiation skills. In HE, one 60-minute group covered HIV/STD disease, testing, treatment, and prevention information. There were a number of USOs at follow-up. A significant difference in mean USOs was obtained between SSB and HE over time ($F = 67.2, P < 0.0001$). At 3 months, significant decrements were observed in both conditions. At 6 months, SSB maintained the decrease and HE returned to baseline ($P < 0.0377$). Women in SSB had 29% fewer USOs than those in HE. The authors concluded that skills building interventions can produce ongoing sexual risk reduction in women in community drug treatment. **Editors' note: Introducing a new acronym - USO or unprotected sex occasion - this randomised controlled trial found sustained sexual risk reduction 6 months later in women on drug treatment who received a brief, gender-specific, skills-oriented risk reduction intervention delivered by drug treatment staff at community-based clinics. The control group received one health education session compared to the five skills building sessions received by the experimental group, a design that does not permit definitive attribution because of difference in doses. Nonetheless, these are impressive results for women who are at high risk for heterosexual acquisition of HIV during drug treatment, as they are often in primary sexual relationships with male drug users and their own substance use may continue, influencing sexual risk.**

5. Biomedical HIV prevention tools

Weiss HA, Wasserheit JN, Barnabas RV, Hayes RJ, Abu-Raddad LJ. Persisting with prevention: The importance of adherence for HIV prevention. *Emerg Themes Epidemiol.* 2008 Jul 11;5:8.

Only four out of 31 completed randomised controlled trials of HIV prevention strategies against sexual transmission have shown significant efficacy. Poor adherence may have contributed to the lack of effect in some of these trials. In this paper Weiss et al explore the impact of various levels of adherence on measured efficacy within a randomized controlled trial. They used simple quantitative methods to illustrate the impact of various levels of adherence on measured efficacy by assuming a uniform population in terms of sexual behaviour and the binomial model for the transmission probability per partnership. At 100% adherence the measured efficacy within a randomised controlled trial is a reasonable approximation of the true biological efficacy. However, as adherence levels fall, the efficacy measured within a trial substantially under-estimates the true biological efficacy. For example, at 60% adherence, the measured efficacy can be less than half of the true biological efficacy. The authors conclude that poor adherence during a trial can substantially reduce the power to detect an effect, and improved methods of achieving and maintaining high adherence within trials are needed. There are currently 12 ongoing HIV prevention trials, all but one of which require ongoing user-adherence. Attention must be given to methods of maximizing adherence when piloting and designing randomised controlled trials RCTs and HIV prevention programmes. **Editors' note: Anticipated levels of adherence to prevention measures, which are likely to be lower than those achieved with antiretroviral treatment, must be taken into account when designing trials. Trials need to be powered to detect a smaller efficacy than a true biological efficacy that would result from 100% adherence. Otherwise it is not clear whether a null result, as has**

been seen in several trials, reflects a truly ineffective intervention; low study power due to factors such as underestimates of HIV incidence, effective intervention in the control arm, and higher than expected loss to follow-up; or poor adherence. Methods to achieve and maintain high adherence in a trial are key to successful trial conduct but also to eventual application of any prevention method that does prove efficacious.

Guest G, Shattuck D, Johnson L, Akumatey B, Clarke EE, Chen PL, Macqueen KM. Changes in Sexual Risk Behavior Among Participants in a PrEP HIV Prevention Trial. *Sex Transm Dis*. 2008 Jul 25. [Epub ahead of print]

One of the concerns raised regarding the introduction of any new HIV-prevention measure, such as pre-exposure prophylaxis (PrEP), is the potential for risk disinhibition or sexual risk compensation. The oral tenofovir HIV prevention trial has been the subject of international discussion in this regard. This article maps the changes in sexual risk behaviour among women participating in the oral tenofovir HIV prevention trial in Ghana. Content-driven, thematic analysis was carried out on qualitative data obtained from in-depth interviews with study participants. Growth curve analysis was the primary method used to document trends over time in self-reported sexual behaviour collected monthly. Overall, the study found that sexual risk behaviour did not increase during the trial. Number of sexual partners and rate of unprotected sex acts decreased across the 12-month period of study enrolment. Certain subgroups of women, however, exhibited different growth curves. Data indicate that the HIV prevention counselling associated with the trial was effective. Guest et al conclude that counselling during the trial was effective. Different types of counselling and messaging may be needed for different subgroups within a population. These findings also have implications for required sample sizes for future HIV prevention trials where seroconversion is the main outcome. **Editors' note: Most biomedical HIV prevention trials anticipate a reduction in risk behaviours in all arms of the trial as participants receive a 'standard of prevention' package including counselling, male and/or female condoms, and other measures. However, risk behaviour may increase if participants either know (as in the male circumcision trials) or believe (in a vaccine, microbicide, or oral pre-exposure prophylaxis trial) that they are in the experimental arm and that the intervention works. Such risk compensation was not seen in the male circumcision trials, other than increased frequency of sex (not increased partners or less condom use) in the Orange Farm trial, and was not seen in this trial of oral pre-exposure prophylaxis in Ghana. Procedures such as consistent counselling and re-consenting participants to reinforce the nature of equipoise in a trial are important in meeting ethical obligations and minimising risk compensation.**

6. Treatment adherence

Cantrell RA, Sinkala M, Megazinni K, Lawso-Marriott S, Washington S, Chi BH, Tambatamba-Chapula B, Levy J, Stringer EM, Mulenga L, Stringer JS. A pilot study of food supplementation to improve adherence to antiretroviral therapy among food-insecure adults in Lusaka, Zambia. *J Acquir Immune Defic Syndr*. 2008 Oct 1;49(2):190-5.

The provision of food supplementation to food-insecure patients initiating antiretroviral therapy (ART) may improve adherence to medications. In a home-based adherence support program at 8 government clinics Cantrell et al assessed patients for food insecurity. Four clinics provided food supplementation, and 4 acted as controls. The analysis compared adherence (assessed by medication possession ratio), CD4, and weight gain outcomes among

food-insecure patients enrolled at the food clinics with those enrolled at the control clinics. Between May 1, 2004, and March 31, 2005, 636 food-insecure adults were enrolled. Food supplementation was associated with better adherence to therapy. Two hundred fifty-eight of 366 (70%) patients in the food group achieved a medication possession ratio of 95% or greater versus 79 of 166 (48%) among controls (relative risk = 1.5; 95% confidence interval: 1.2 to 1.8). This finding was unchanged after adjustment for sex, age, baseline CD4 count, baseline World Health Organization stage, and baseline haemoglobin. The authors did not observe a significant effect of food supplementation on weight gain or CD4 cell response. This analysis suggests that providing food to food-insecure patients initiating ART is feasible and may improve adherence to medication. A large randomized study of the clinical benefits of food supplementation to patients on antiretroviral treatment is urgently needed to inform international policy. **Editors' note: Poor nutrition can undermine adherence by potentiating drug toxicity and making people too tired to travel to the pharmacy to obtain medications. With one third of Zambians and almost half of people on antiretroviral treatment in Zambia 'food insecure', meaning lacking consistent access to enough food of sufficient variety to meet dietary needs, the findings of this randomised study of food supplementation for households in which a person on antiretroviral treatment resides are important. External funding from donors that is earmarked for HIV treatment in similar settings should include a food supplementation component in the interests of improved patient adherence to medication.**

Amberbir A, Woldemichael K, Getachew S, Girma B, Deribe K. Predictors of adherence to antiretroviral therapy among HIV-infected persons: a prospective study in Southwest Ethiopia. *BMC Public Health*. 2008 Jul 30;8:265.

The devastating impact of AIDS in the world especially in sub-Saharan Africa has led to an unprecedented global effort to ensure access to antiretroviral treatment drugs (ART). Given that medication-taking behaviour can immensely affect an individual's response, ART adherence is now widely recognized as an 'Achilles heel' for the successful outcome. The present study was undertaken to investigate the rate and predictors of adherence to antiretroviral therapy among HIV-infected persons in southwest Ethiopia. The study was conducted in the antiretroviral therapy unit of Jimma University Specialized Hospital. A prospective study was undertaken on a total of 400 HIV infected persons. Data were collected using a pre-tested interviewer-administered structured questionnaire at first month (M0) and third month (M3) follow up visits. A total of 400 and 383 patients at baseline (M0) and at follow up visit (M3) respectively were interviewed. Self-reported dose adherence in the study area was 94.3%. The rate considering the combined indicator (dose, time and food) was 75.7%. Within a three month follow up period, dose adherence decreased by 2% and overall adherence rate decreased by more than 3%. Adherence was common in those patients who have a social support (OR, 1.82, 95%CI, 1.04, 3.21). Patients who were not depressed were two times more likely to be adherent than those who were depressed (OR, 2.13, 95%CI, 1.18, 3.81). However, at the follow up visit, social support (OR, 2.42, 95%CI, 1.29, 4.55) and the use of memory aids (OR, 3.29, 95%CI, 1.44, 7.51) were found to be independent predictors of adherence. The principal reasons reported for skipping doses in this study were simply forgetting, feeling sick or ill, being busy and running out of medication in more than 75% of the cases. The self reported adherence rate was high in the study area. The study showed that adherence is a dynamic process which changes overtime and cannot reliably be predicted by a few patient characteristics that are assumed to vary with time.

Adherence is a process, not a single event, and adherence support should be integrated into regular clinical follow up. **Editors' note: Adherence studies often focus on 'dose adherence' but for successful antiretroviral treatment, adherence to scheduling and dietary instructions are important components of adherence. The results of this study from Ethiopia, which used a combined indicator, suggest a positive role for memory aids and highlight the importance of discussions about the sources of social support and possible solutions prior to starting antiretroviral treatment.**

7. *Diagnostics*

Mee P, Fielding KL, Charalambous S, Churchyard GJ, Grant AD. Evaluation of the WHO criteria for antiretroviral treatment failure among adults in South Africa. *AIDS*. 2008 Oct 1;22(15):1971-7.

Mee et al assessed the performance of WHO clinical and CD4 cell count criteria for antiretroviral treatment (ART) failure among HIV-infected adults in a workplace HIV care programme in South Africa. This cohort study included initially ART-naive participants who remained on first-line therapy and had an evaluable HIV viral load result at the 12-month visit. WHO-defined clinical and CD4 cell count criteria for ART failure were compared against a gold standard of virological failure. The authors found that among 324 individuals (97.5% men, median age 40.2, median starting CD4 cell count and viral load 154 cells/ml and 47,503 copies/ml, respectively), 33 (10.2%) had definite or probable virological failure at 12 months, compared with 19 (6.0%) and 40 (12.5%) with WHO-defined CD4 and clinical failure, respectively. CD4 criteria had a sensitivity of 21.2% and a specificity of 95.8% in detecting virological failure, and clinical criteria had sensitivity of 15.2% and specificity of 88.1%. The positive predictive value of CD4 and clinical criteria in detecting virological failure were 36.8 and 12.8%, respectively. Exclusion of weight loss or tuberculosis failed to improve the performance of clinical criteria. The authors concluded that WHO clinical and CD4 criteria have poor sensitivity and specificity in detecting virological failure. The low specificities and positive predictive values mean that individuals with adequate virological suppression risk being incorrectly classified as having treatment failure and unnecessarily switched to second-line therapy. Virological failure should be confirmed before switching to second-line therapy. **Editors' note: This study raises important questions about current WHO clinical and CD4 count criteria for detecting virological failure and switching to second line therapy. The high number of false positive findings translates into a low positive predictive value, meaning that patients will be switched even though in reality they have adequately suppressed viral loads. This speaks strongly in favour of improved access to viral load testing in resource-constrained settings, although the public health approach may still suggest preserving second line regimens until progressively falling CD4 counts make it absolutely essential to switch. The counter argument is that maintaining individuals on failing regimens may lead to increased risk of transmission of resistant virus.**

Amellal B, Murphy R, Maiga A, Brucker G, Katlama C, Calvez V, Marcelin A. Stability of HIV RNA in plasma specimens stored at different temperatures. *HIV Med*. 2008 Aug 27. [Epub ahead of print]

In resource-limited countries, HIV-1 RNA quantification is usually performed in reference laboratories. Samples from remote areas are transported under suboptimal conditions. Here Amellal et al evaluated HIV-1 RNA stability in plasma stored at different temperatures for 1

week. Blood samples collected in ethylenediaminetetraacetic acid (EDTA) and processed within 6 hours of collection were tested by HIV-1 RNA quantification using Roche Cobas Ampliprep-Cobas TaqMan((R)) (Roche Diagnostics). The results were compared with matched HIV-1 RNA concentrations determined from plasma stored for 1 week at 4, 22, 30 or 37 degrees C. A total of 51 samples were evaluated: 10 stored at 4 degrees C, 15 at 22 degrees C, 16 at 30 degrees C and 10 at 37 degrees C. Keeping plasma at 4, 22 or 30 degrees C for 1 week did not affect HIV RNA measurement. Compared with HIV-1 RNA concentrations determined from fresh plasma, the correlation was significant for each of the three temperatures with no RNA decay. In contrast, HIV-1 RNA levels decreased significantly when plasma was stored at 37 degrees C. The 10 samples submitted at this temperature showed a weaker correlation ($\rho=0.84$; $P=0.012$) and a significantly reduced median HIV-1 RNA concentration ($-0.92 \log_{10}$ HIV-1 RNA copies/mL; $P=0.005$). Plasma can be saved for up to 1 week at 30 degrees C before shipping to a reference laboratory for HIV-1 RNA quantification. **Editors' note: Generally speaking, biological specimens should be processed as soon as possible and then either stored or transported for testing under optimal conditions. These encouraging findings of stability of HIV RNA concentrations in fresh plasma at up to 30 C are encouraging but cannot be extrapolated to whole blood specimens. Further research is needed to determine under what conditions plasma processing before transport of specimens to reference laboratories is essential. Point-of-care tests for CD count and viral load would be an even better solution.**

8. Basic science

Worobey M, Gemmel M, Teuwen DE, Haselkorn T, Kunstman K, Bunce M, Muyembe JJ, Kabongo JM, Kalengayi RM, Van Marck E, Gilbert MT, Wolinsky SM. Direct evidence of extensive diversity of HIV-1 in Kinshasa by 1960. *Nature*. 2008 Oct 2;455(7213):661-4.

Human immunodeficiency virus type 1 (HIV-1) sequences that pre-date the recognition of AIDS are critical to defining the time of origin and the timescale of virus evolution. A viral sequence from 1959 (ZR59) is the oldest known HIV-1 infection. Other historically documented sequences, important calibration points to convert evolutionary distance into time, are lacking, however; ZR59 is the only one sampled before 1976. Here Worobey et al report the amplification and characterization of viral sequences from a Bouin's-fixed paraffin-embedded lymph node biopsy specimen obtained in 1960 from an adult female in Léopoldville, Belgian Congo (now Kinshasa, Democratic Republic of the Congo (DRC)), and they use them to conduct the first comparative evolutionary genetic study of early pre-AIDS epidemic HIV-1 group M viruses. Phylogenetic analyses position this viral sequence (DRC60) closest to the ancestral node of subtype A (excluding A2). Relaxed molecular clock analyses incorporating DRC60 and ZR59 date the most recent common ancestor of the M group to near the beginning of the twentieth century. The sizeable genetic distance between DRC60 and ZR59 directly demonstrates that diversification of HIV-1 in west-central Africa occurred long before the recognized AIDS pandemic. The recovery of viral gene sequences from decades-old paraffin-embedded tissues opens the door to a detailed palaeovirological investigation of the evolutionary history of HIV-1 that is not accessible by other methods. **Editors' note: This is like a detective story which starts with finding old specimens from Kinshasa that both contain HIV and are in good enough shape for analysis. This genetic sequencing comparison reveals that HIV-1 group M, which still exists as a natural reservoir in chimpanzees in the same region, likely crossed species near the beginning of the 20th century. Rather than fading away, HIV in humans then may have taken off**

with the founding and growth of colonial administrative and trading centres like Kinshasa. Further work on the evolutionary history of HIV could yield important insights into the pathogenesis, virulence, and evolution of HIV.

Bailey JR, O'Connell K, Yang HC, Han Y, Xu J, Jilek B, Williams TM, Ray SC, Siliciano RF, Blankson JN. Transmission of HIV-1 from a Patient Who Developed AIDS to an Elite Suppressor. *J Virol*. 2008 May 21. [Epub ahead of print]

Elite suppressors are untreated HIV-1 infected patients who maintain viral loads of < 50 copies/ml. The mechanisms involved in this control of viral replication remain unclear. Prior studies have suggested that these patients, as well as long-term non-progressors (LTNP), are infected with defective HIV-1 variants. Other reports have shown that the HLA-B*27 and B*57 alleles are overrepresented in these patients, suggesting that host factors play a role in the control of viral replication. In order to distinguish between these hypotheses, Bailey et al studied differences in viral isolates and immune responses of an HIV-1 transmission pair. While both patients are HLA-B*57 positive, the transmitter progressed to AIDS whereas the recipient, who is also HLA-B*27 positive, is an elite suppressors. Isolates from both patients were replication-competent and contained the T242N escape mutation in Gag which is known to decrease viral fitness. While the acquisition of compensatory mutations occurred in isolates from the progressor, a superior HIV-specific CD8(+) T cell response in the elite suppressors appears to have prevented viral replication and thus the evolution towards a more fit variant. In addition, CD8(+) T cells in the elite suppressors have selected for a rare mutation in an immunodominant HLA-B*27 restricted Gag epitope which also has a negative impact on fitness. The results strongly suggest that through direct and indirect mechanisms, CD8(+) T cells in some elite suppressors control HIV-1 isolates that are capable of causing profound immunosuppression. **Editors' note: This is an intriguing story. These two people were infected by the same virus although the actual date of transmission between them is unknown. They had been sexual partners for 17 years before the diagnosis of AIDS was made in the index case 10 years ago and subsequent positive HIV test result in his partner. He had progressed to AIDS but she was able to suppress the virus. She had the advantage of the HLA-B*27 allele but above all she had a superior CD8+ T-cell response that stopped the virus from becoming more fit. Now if we could develop a vaccine that elicited similar CD8* T cell responses we would have a therapeutic vaccine for the treatment armamentarium.**

9. Surveillance

Lyerla R, Gouws E, Garcia-Calleja JM. The quality of sero-surveillance in low- and middle-income countries: status and trends through 2007. *Sex Transm Infect*. 2008 Aug;84 Suppl 1:i85-i91.

Lyerla et al examined the quality of HIV sero-surveillance systems in 127 low-income and middle-income countries by 2007, as well as gaps in data needed for reliable estimates of HIV prevalence and size of populations at risk for infection. They scored quality of countries' surveillance systems using information from 2001 through 2007. Sero-surveillance data were compiled from the US Census Bureau's HIV/AIDS Surveillance Database, from countries' national HIV surveillance reports available to UNAIDS, from demographic and health survey (DHS) data, from the scientific literature, and from countries' Estimation and Projection Programme (EPP) data files. The quality of systems was scored according to the classification of the epidemic in each country (generalised, concentrated, or low-level). The

authors found that the number of countries that were categorised as fully functioning in 2007 was 40. Forty-three countries were identified as partially functioning while 44 were categorised as poorly functioning. Low scores were most often attributed to a lack of recent data or lack of data from appropriate risk populations. They concluded that many countries still have poorly functioning surveillance systems. The inclusion of HIV testing in national population-based surveys in recent years has resulted in some countries with generalised epidemics receiving higher coverage scores, but many countries with concentrated or low-level epidemics continue to lack data on populations at higher risk of HIV. **Editors' note: This review found wide variations in the quality of surveillance systems monitoring the HIV epidemic both within and across regions. Two-thirds of the countries evaluated had weaknesses. Even countries that had information about marginalised populations at risk of HIV exposure did not have consistent data collection over time to make trend analysis possible. To act on the challenge to 'Know your epidemic, know your response', many countries need to strengthen HIV surveillance systems while intensifying prevention programmes - the two go hand in hand for effective responses.**

Montana LS, Mishra V, Hong R. Comparison of HIV prevalence estimates from antenatal care surveillance and population-based surveys in sub-Saharan Africa. *Sex Transm Infect.* 2008 Aug;84 Suppl 1:i78-i84.

Montana et al aimed to compare HIV seroprevalence estimates obtained from antenatal care (ANC) sentinel surveillance surveys in Ethiopia, Kenya, Malawi, Tanzania and Uganda with those from population-based demographic and health surveys (DHS) and AIDS indicator surveys (AIS). Geographical information system methods were used to map ANC surveillance sites and DHS/AIS survey clusters within a 15-km radius of the ANC sites. National DHS/AIS HIV prevalence estimates for women and men were compared with national prevalence estimates from ANC surveillance. DHS/AIS HIV prevalence estimates for women and men residing within 15 km of ANC sites were compared with those from ANC surveillance. For women, these comparisons were also stratified by current pregnancy status, experience of recent childbirth and receiving ANC for the last birth. In four of the five countries, national DHS/AIS estimates of HIV prevalence were lower than the ANC surveillance estimates. Comparing women and men in the catchment areas of the ANC sites, the DHS/AIS estimates were similar to ANC surveillance estimates. DHS/AIS estimates for men residing in the catchment areas of ANC sites were much lower than ANC surveillance estimates for women in all cases. ANC estimates were higher for younger women than DHS/AIS estimates for women in ANC catchment areas, but lower at older ages. In all cases, urban prevalence was higher than rural prevalence but there were no consistent patterns by education. The authors concluded that ANC surveillance surveys tend to overestimate HIV prevalence compared to prevalence among women in the general population in DHS/AIS surveys. However, the ANC and DHS/AIS estimates are similar when restricted to women and men, or to women only, residing in catchment areas of ANC sites. Patterns by age and urban/rural residence suggest possible bias in the ANC estimates. **Editors' note: More countries experiencing generalised HIV epidemics are choosing to conduct national DHS-plus surveys in which HIV status is linked to demographic and health information through the addition of non-nominal testing. Triangulating DHS-plus findings with other data sources such as antenatal surveillance can help provide a more accurate window on the overall extent of a country's HIV epidemic but antenatal surveillance will continue to provide important trend data.**

10. Women's Health

Denny L, Boa R, Williamson AL, Allan B, Hardie D, Stan R, Myer L. Human Papillomavirus Infection and Cervical Disease in Human Immunodeficiency Virus-1-Infected Women. *Obstet Gynecol.* 2008 Jun;111(6):1380-1387.

Denny et al report on the natural history of high-risk human papillomavirus (HPV) infection and cervical disease in human immunodeficiency virus (HIV)-1-infected women living in Cape Town, South Africa. They studied prospectively 400 untreated, HIV-1-infected women who underwent high-risk HPV DNA testing, cytology, colposcopy, histology, and CD4 count testing every 6 months for 36 months. Human immunodeficiency virus viral loads and HPV type distribution were determined at entry and after 18 months. Sixty-eight percent of the women were high-risk HPV DNA positive at entry, 35% had a cytologic diagnosis of low-grade squamous intraepithelial lesion (LSIL), and 13% had high-grade squamous intraepithelial lesion (HSIL). There were no cancers. Abnormal cytology and high-risk HPV positivity were strongly correlated with low CD4 counts and high HIV viral loads. The most prevalent types of HPV were HPV-16, -52, -53, -35, and -18. Incident high-risk HPV infection occurred in 22%, and of those infected with high-risk HPV, 94% of infections persisted over an 18-month period, and 6% cleared their infections. Cytologic progression to SIL from normal/atypical squamous cells of undetermined significance cytology occurred in 17% of cases, but only 4% of cases of LSIL progressed to HSIL. Denny et al concluded that there is a high level of high-risk HPV infection in HIV-1 infected women, but progression to HSIL over 36 months occurred in the minority of cases. They recommend an initial coloscopy for an abnormal test, and if no high-grade lesion is identified, triennial screening would be appropriate. Human papillomavirus type 16 was the commonest, and HPV-18 was the fifth commonest, suggesting that vaccination against these two types would have a significant effect. LEVEL OF EVIDENCE: II. **Editors' note: These findings of high-risk HPV infection in more than two-thirds of 400 women living with HIV and abnormal cervical cytology in 55% of them at baseline in this 3 year study are concerning. The study found that HPV-associated disease was strongly influenced by immune status, as reflected in CD4 counts and viral loads, suggesting that antiretroviral treatment can play an important role in preventing progression to cervical cancer.**

Jarrin I, Geskus R, Bhaskaran K, Prins M, Perez-Hoyos S, Muga R, Hernández-Aguado I, Meyer L, Porter K, del Amo J; CASCADE Collaboration. Gender differences in HIV progression to AIDS and death in industrialized countries: slower disease progression following HIV seroconversion in women. *Am J Epidemiol.* 2008 Sep 1;168(5):532-40. Epub 2008 Jul 28.

To evaluate sex differences in human immunodeficiency virus (HIV) disease progression before (pre-1997) and after (1997-2006) introduction of highly active antiretroviral therapy, the authors used data from a collaboration of 23 HIV seroconverter cohort studies from Europe, Australia, and Canada restricted to the 6,923 seroconverters infected through injecting drug use and sex between men and women. Within a competing risk framework, they used Cox proportional hazards models allowing for late entry to evaluate sex differences in time from HIV seroconversion to death, to acquired immunodeficiency syndrome (AIDS), and to each first AIDS-defining disease and death without AIDS. While no significant sex differences were found before 1997, from 1997 onward, women had a lower risk of AIDS (adjusted cumulative relative risk (aCRR) = 0.76, 95% confidence interval (CI): 0.63, 0.90) and death (adjusted hazard ratio = 0.68, 95% CI: 0.56, 0.82) than men did. Compared with men, women also had lower risks of AIDS dementia complex (aCRR = 0.23, 95% CI: 0.07,

0.74), tuberculosis (aCRR = 0.60, 95% CI: 0.39, 0.92), Kaposi's sarcoma (aCRR = 0.27, 95% CI: 0.07, 0.99), lymphomas (aCRR = 0.47, 95% CI: 0.23, 0.96), and death without AIDS (aCRR = 0.74, 95% CI: 0.56, 0.98). Sex differences in HIV disease progression have become larger and statistically significant in the era of highly active antiretroviral therapy, supporting a stronger impact of health interventions among women. **Editors' note: This is the first study to examine sex differences in male and female seroconverters in the same transmission category. From 1997 onward, women had a lower mortality than men for both all-cause mortality and death without AIDS. These findings confirm those from European settings but not studies in the United States that have shown higher accident or injury-related mortality in women with HIV than in men and no reductions in overall mortality for women with HIV after the advent of antiretroviral treatment. These discrepancies may be due to stark socioeconomic differences between study populations, inclusion or exclusion of gay men, and differences in health care systems between Europe and the United States.**

11. Cultural determinants of risk

Ayikukwei R, Ngare D, Sidle J, Ayuku D, Baliddawa J, Greene J. HIV/AIDS and cultural practices in western Kenya: the impact of sexual cleansing rituals on sexual behaviours. *Cult Health Sex*. 2008 Aug;10(6):587-99.

This paper reports on an exploratory study examining the role of sexual cleansing rituals in the transmission of HIV among the Luo community in western Kenya. Data were collected using both in-depth interviews and focus group discussions. The study population consisted of 38 widows, 12 community elders and 44 cleansers. Data were collected on non-behavioural causes, behavioural causes, and behavioural indicators associated with sexual rituals. Content analysis revealed five central themes: the effect of the ritual on sexual behaviours; factors contributing to the continued practice of the ritual, including a sub-theme on the commercialization of the ritual; the inseparable relationship between the sanctity of sex, prosperity and fertility of the land; and the effects of modernization on the ritual, including a sub-theme on the effects of mass media on HIV-prevention awareness campaigns. Causal factors of unchanging sexual behaviours are deeply rooted in traditional beliefs, which the community uphold strongly. These beliefs encourage men and women to have multiple sexual partners in a context where the use of condoms is rejected and little HIV testing is carried out. **Editors' note: Nyanza Province has the highest HIV prevalence in Kenya. This study concludes that the Luo community feels vulnerable because it has not been able yet to devise systems that strike a balance between honouring tradition and protecting the community against HIV. And yet, culture is not immutable - it can change in response to changing circumstances. A month ago, several male Luo politicians reported publicly that they were circumcised when it is Luo tradition to not be circumcised. In Kisumu, the waiting lines for circumcision services continue to grow as young men value the promise of partial protection against HIV that circumcision can afford over the view that being non-circumcised is essential to cultural and community identity. The role of sexual cleansing in the middle of a generalised epidemic may also come under scrutiny by the community in the not so distant future.**

That was *HIV this week*, signing off.

Editors' notes on journal access:

For readers in all countries:

All abstracts in *HIV This Week* are freely available on the Web.

You can access a majority of scientific journals free of charge no matter where you are located, but for some journals you do need a subscription to access the full text of an article. Some journals are free to readers in all countries either through ScienceDirect or through the journal's own website.

For articles available through ScienceDirect, you should follow the link <http://www.sciencedirect.com/> to the ScienceDirect home page. Then click on journals and look for the title of the journal you are searching for.

Some journals are open access, available to readers in all countries: American Medical Association journals (<http://pubs.ama-assn.org/>), American Society of Clinical Oncology (2 journals), Australian Medical Association (1 journal), BioMed Central journals (<http://www.biomedcentral.com/>), BMJ journals (<http://journals.bmj.com/>), Canadian Medical Association (1 journal), Nature Publishing Group journals (<http://www.nature.com/>), Public Library of Science journal (<http://medicine.plosjournals.org/>) and Science (1 journal).

Other journals offer free access to full-text articles after a certain period of time (see lists at High Wire Press <http://highwire.stanford.edu/lists/freeart.dtl> and PubMed Central <http://www.pubmedcentral.nih.gov/>).

For residents of low- and middle-income countries: the Health InterNetwork Access to Research Initiative (HINARI)

HINARI, set up by the World Health Organisation (WHO) and major publishers, enables readers in low- and middle-income countries to gain access to one of the world's largest collections of biomedical and health literature. Over 3400 journal titles are now available to health institutions in 113 countries, benefiting many thousands of health workers and researchers, and in turn, contributing to improved world health. More information on the HINARI programme and eligible countries is available at <http://www.who.int/hinari/en/>
Email: hinari@who.int

Local, not-for-profit institutions in low- and middle- income countries may register for access to the journals through HINARI. Institutions in countries with GNP per capita below \$1000 are eligible for free access. Institutions in countries with GNP per capita \$1000-\$3000 pay a fee of \$1000 per year/institution.

For employees of UNAIDS or WHO:

If you work for WHO or UNAIDS in Geneva, you can access a number of journals by going to the WHO library. You can also see the full list of journals you can access freely on the web (including usernames and passwords) by going to the WHO Library website, accessible through the homepage of WHO intranet <https://intranet.who.int/> under information resources. If you work for UNAIDS *HIV This Week* is also available on the intranet at the link <https://intranet.unaids.org/HIVThisWeek/2007/index.htm>.

