

HIV This Week: what scientific journals said

Welcome to the 68th issue of *HIV This Week*! In this issue, we cover **herpes simplex virus-2** (male circumcision helpful yet again; insights on the complex relationship of bed partners HSV-2 and HIV), **national responses** (the fallout of fragile treatment delivery in Serbia and Montenegro; sustaining the Cambodian 100% condom use programme in the face of high sex worker turnover; prevention of sexually transmitted infections and HIV in the Países Africanos de Língua Oficial Portuguesa: Mozambique, Angola, Cape Verde, Guinea-Bissau, Equatorial Guinea, and São Tomé and Príncipe), **tuberculosis** (exciting developments as guinea pigs demonstrate that upper-room ultraviolet light prevents tuberculosis transmission; everything we know about extensively drug-resistant tuberculosis), **people living with HIV** (a trial of long-term testosterone administration in HIV-infected women shows marked benefits; required reading: what you need to know to travel safely), **treatment adherence** (adolescents in 9 countries need adherence support; is it treatment access or adherence that transportation costs affect in Uganda?; stock outs and non-adherence to subsidized treatment in southeast Nigeria), **prevention of mother-to-child transmission** (a role for rapid testing during labour and delivery?; early knowledge of babies' HIV status in Soweto but need to improve infant feeding advice and family planning counselling), **injecting drug use** (high time for harm reduction in Hyderabad and Sukkur, Pakistan), **prognosis** (symptoms while "asymptomatic"; how weight gain at 3 months after starting antiretroviral therapy in Kenya and Cambodia predicts survival), **reproductive health** (fertility choices and infertility treatment for women living with HIV), **basic science** (elite controllers reveal a broad diversity of neutralizing antibodies isolated from memory B cells; premature aging of T cells and faster disease progression), and **positive prevention** (a review of published research in this 10 year old field; how to use formative research to design programmes for prisoners with HIV who are transitioning to the community).

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1. Herpes simplex

Tobian AAR, Serwadda D, Quinn TC, Kigozi G, Gravitt PE, Laeyendecker O, Charvat B,* Ssempijja V, Riedesel M, Oliver AE, Nowak RG, Moulton LH, Chen MZ, Reynolds SJ, Wawer MJ and Gray RH. Male Circumcision for the Prevention of HSV-2 and HPV Infections and Syphilis. *N Engl J Med*. 2009;360:1298-309.

Male circumcision significantly reduced the incidence of human immunodeficiency virus (HIV) infection among men in three clinical trials. Tobian and colleagues assessed the efficacy of male circumcision for the prevention of herpes simplex virus type 2 (HSV-2) and human papillomavirus (HPV) infections and syphilis in HIV-negative adolescent boys and men. They enrolled 5534 HIV-negative, uncircumcised male subjects between the ages of 15 and 49 years in two trials of male circumcision for the prevention of HIV and other sexually transmitted infections. Of these subjects, 3393 (61.3%) were HSV-2- seronegative at enrolment. Of the seronegative subjects, 1684 had been randomly assigned to undergo immediate circumcision (intervention group) and 1709 to undergo circumcision after 24 months (control group). At baseline and at 6, 12, and 24 months, the authors tested subjects for HSV-2 and HIV infection and syphilis, along with performing physical examinations and conducting interviews. In addition, they evaluated a subgroup of subjects for HPV infection at baseline and at 24 months. At 24 months, the cumulative probability of HSV-2 seroconversion was 7.8% in the intervention group and 10.3% in the control group (adjusted hazard ratio in the intervention group, 0.72; 95% confidence interval [CI], 0.56 to 0.92; P = 0.008). The prevalence of high-risk HPV genotypes was 18.0% in the intervention group and 27.9% in the control group (adjusted risk ratio, 0.65; 95% CI, 0.46 to 0.90; P = 0.009). However, no significant difference between the two study groups was observed in the incidence of syphilis (adjusted hazard ratio, 1.10; 95% CI, 0.75 to 1.65; P = 0.44). In addition to decreasing the incidence of HIV infection, male circumcision significantly reduced the incidence of HSV-2 infection and the prevalence of HPV infection, findings that underscore the potential public health benefits of the procedure. **Editors' note: To date, limited statistical power, confounding by sexual practices correlated with a high risk of transmission, and determination of circumcision status only by self-report have plagued observational studies on male circumcision and sexually transmitted infections. This randomised, controlled trial in rural Uganda demonstrates that male circumcision in adolescent boys and men significantly reduces the incidence of herpes simplex virus-2 (HSV-2) infection and the prevalence of human papilloma virus (HPV) infection. Whether the latter is due to decreased HPV acquisition or increased HPV clearance is unclear but it does explain the lower risk of cervical cancer experienced by women whose partners are circumcised. The adjusted efficacy of male circumcision was 28% for the prevention of HSV-2, an infection thought to be a cofactor in HIV acquisition. This may explain in part the incontrovertible partial protection from HIV afforded by male circumcision.**

Delany-Moretlwe S, Lingappa JR and Celum C. New Insights on Interactions Between HIV-1 and HSV-2. *Curr Infect Dis Rep*. 2009;11(2):135-42.

Herpes simplex type 2 (HSV-2) infection is common and frequently asymptomatic. Concerns exist about the high prevalence of HSV-2, particularly in areas of high HIV prevalence, because of observations that HSV-2 is associated with an increased risk of HIV acquisition, transmission, and disease progression. Several randomized trials have tested or are testing whether HSV-2 treatment can limit the spread of HIV, with mixed results. Although

treatment with acyclovir, 400 mg twice daily, does not reduce HIV incidence, suppressive acyclovir and valacyclovir reduce HIV levels in plasma and in the genital tract. Ongoing trials are evaluating whether HSV suppression will reduce HIV transmission and disease progression. Until a protective HSV-2 or HIV vaccine is available, effective interventions that reduce the effect of HSV-2 on HIV transmission are critically needed. **Editors' note: This excellent summary of what is known about the complex and bidirectional interactions between HIV-1 and herpes simplex virus-2 (HSV-2) was published before the May 8th release of results from the multi-centre Partners in Prevention Study of 3408 discordant couples conducted in Botswana, Kenya, Rwanda, South Africa, Tanzania, Uganda and Zambia. To test whether HSV-2 daily suppressive therapy would reduce HIV transmission, HIV/HSV-2 co-infected partners were randomised to receive acyclovir 400 mg twice daily or matching placebo for 2 years while the uninfected partner was followed-up for HIV-1 seroconversion. Although acyclovir reduced the frequency of genital ulcers by 73% and HIV viral load by 40%, no significant difference was found in the rate of HIV transmission. A 17% reduction in HIV disease progression produced by low cost acyclovir was an intriguing result worthy of further study. With more than half a billion people infected with HSV-2, including up to 90% of people living with HIV, developing an HSV-2 vaccine continues to be a very high priority.**

2. National responses

Bernays S, Rhodes T. Experiencing uncertain HIV treatment delivery in a transitional setting: qualitative study. *AIDS Care*. 2009;21(3):315-21.

Advances in HIV treatment availability mean that the promise of highly active anti-retroviral treatment to turn HIV into a manageable chronic illness is becoming a reality for millions. However the mutability of the virus means that treatment adherence demands are high, and the supply of these life-saving treatments needs to be constant. The onus is generally placed on the individual to adhere, and there is little focus in research or policy on the state's adherence to delivering treatment consistently. Bernays and colleagues undertook in-depth qualitative interviews to explore the narratives of HIV treatment experience among 41 people living with HIV and 18 HIV treatment service providers in Serbia and Montenegro, a transitional setting in which state delivered and funded HIV treatment is inconsistently available. Data were analysed inductively and thematically. Treatment shortages were common so the delivery of appropriate HIV treatment was not continuous. Access to reliable treatment and supply forecast information was weak and uneven. The insecure treatment situation fostered significant anxiety amongst people living with HIV. In the absence of reliable and sustained treatment access, information, and support, people living with HIV absorb the anxieties of system failures. This uncertainty led to an individuation of "treatment". People living with HIV adopted rationing strategies to mediate their anxiety, energy and hope. This predominately resulted in varying forms of disengagement and neglect for social change. It is likely that this has significant negative implications for the promotion of HIV treatment advocacy and anti-stigma efforts. **Editors' note: Adherence literature to date has focused primarily on patient adherence to treatment regimens rather than on the social and psychological effects of involuntary treatment interruptions. Fragile treatment delivery undermines the quality of life and capacity of people living with HIV to manage it as a manageable, chronic illness. Although some people in this study reduced their anxiety by fostering networks and resources to gain access to information and treatment, a form of social capital to generate security, others withdrew, trusting**

no one but their treatment provider and becoming less likely to disclose to others. This research highlights the clear need for a social science of scale-up.

Sopheab H, Morineau G, Neal JJ, Saphonn V, Fylkesnes K. Sustained high prevalence of sexually transmitted infections among female sex workers in Cambodia: high turnover seriously challenges the 100% Condom Use Programme. *BMC Infect Dis.* 2008;8:167.

Cambodia's 100% Condom-Use Programme, implemented nationally in 2001, requires brothel-based female sex workers to use condoms with all clients. In 2005, Sopheab et al conducted a sexually transmitted infection survey among female sex workers. This paper presents sexually transmitted infection prevalence and related risk factors, and discusses prevalence trends in the context of the 100% Condom-Use Programme in Cambodia. From March-May, 1079 female sex workers from eight provinces consented to participate, provided specimens for syphilis, chlamydia, and gonorrhoea testing, and were interviewed. Univariate and multivariate logistic regression analysis was used to determine factors associated with sexually transmitted infections. The prevalence of sexually transmitted infection was compared with data from the 1996 and 2001 sexually transmitted infection surveys. Most female sex workers were young (55% aged 15-24) and new to sex work (60% had worked 12 <or= months). Consistent condom use with clients was reported by 80% of female sex workers, but only 38% of female sex workers always used condoms with sweethearts or casual partners. Being new to sex work was the only factor significantly associated with "any sexually transmitted infection" (OR = 2.1). Prevalence of syphilis was 2.3%; chlamydia, 14.4%; gonorrhoea, 13.0%; and any sexually transmitted infection, 24.4%. Prevalence of each sexually transmitted infection in 2005 was significantly lower than in 1996, but essentially the same as prevalence observed in 2001. New female sex workers were found to have substantially higher prevalence than those with longer experience. The percent of female sex workers who used condoms consistently was high with clients but remained low with non-paying sex partners. Because of the high turnover of female sex workers, the prevention needs of new female sex workers should be ascertained and addressed. Despite 100% Condom-Use Programme implementation, the prevalence of sexually transmitted infections among female sex workers was the same in 2005 as it was in 2001. Limited coverage and weak implementation capacity of the programme along with questionable quality of the sexually transmitted infection services are likely to have contributed to the sustained high prevalence. The programme should be carefully reviewed in terms of intensity, quality, and coverage. **Editors' note: Successful 100% condom use programmes in Thailand in late 1989 and Cambodia in late 1998 were rigorously conducted with high coverage and intensity. Sustaining such results given the high turnover among sex workers requires regular evaluations of programme quality and impact. Using curable bacterial sexually transmitted infection prevalence makes sense as they are good biological markers reflecting recent risk behaviour but different data collection methods, specimen-sampling techniques, and laboratory methods can make comparison of survey results hazardous. One thing is clear - Cambodia's 100% condom-use programme, implemented nationally in 2001, should focus attention on ascertaining and addressing the prevention needs of new sex workers.**

Monteiro S. STD/AIDS prevention in Portuguese-speaking Africa: a review of the recent literature in the social sciences and health. *Cad Saude Publica.* 2009;25(3):680-6.

The article reviews academic literature in the social sciences and health on the problems and challenges of sexually transmitted diseases and HIV prevention in Portuguese-speaking

African countries. Based on a bibliographic survey of the SciELO, PubMed, and Sociological Abstracts databases between 1997 and 2007, the research under review was organized into two groups, according to content. The first group of studies sought to understand sexually transmitted diseases and HIV vulnerability among social groups by examining local cultural and socioeconomic factors as related to gender dynamics, sexuality, colour/race, religion and health care. The second group encompassed critical assessments of shortcomings in the sexually transmitted diseases and HIV educational messages delivered by governments and international agencies. Attention is called to the way in which the presence of traditional medicine systems and the occurrence of civil wars in the post-colonial period affect the sexually transmitted diseases and HIV epidemic in the African countries under study.

Editors' note: The Portuguese-speaking African countries, known by the acronym PALOP (Países Africanos de Língua Oficial Portuguesa) are Mozambique, Angola, Cape Verde, Guinea-Bissau, Equatorial Guinea, and São Tomé and Príncipe. Although there are cultural and socio-economic similarities between these countries, appreciation of local contexts is critical to understanding how healthcare practices, gender roles, and the interpretation of prevention messages are mediated locally by cultural dynamics and socio-economic and political contexts. This review suggests that demystifying condom use in a pragmatic CNN approach (condoms, needles, and negotiation) as opposed to the moralizing ABC approach (abstinence, be faithful, and condoms for marginalized populations), along with frank and open discussions of sexuality in public fora and the media, would achieve positive results, particularly if accompanied by advances in citizenship rights and equal opportunities.

3. Tuberculosis

Escombe AR, Moore DA, Gilman RH, Navincopa M, Ticona E, Mitchell B, Noakes C, Martínez C, Sheen P, Ramirez R, Quino W, Gonzalez A, Friedland JS, Evans CA. Upper-room ultraviolet light and negative air ionization to prevent tuberculosis transmission. *PLoS Med.* 2009;6(3):e43.

Institutional tuberculosis (TB) transmission is an important public health problem highlighted by the HIV pandemic and the emergence of multidrug- and extensively drug-resistant TB. Effective TB infection control measures are urgently needed. Escombe et al evaluated the efficacy of upper-room ultraviolet (UV) lights and negative air ionization for preventing airborne TB transmission using a guinea pig air-sampling model to measure the TB infectiousness of ward air. For 535 consecutive days, exhaust air from an HIV-TB ward in Lima, Peru, was passed through three guinea pig air-sampling enclosures each housing approximately 150 guinea pigs, using a 2-d cycle. On UV-off days, ward air passed in parallel through a control animal enclosure and a similar enclosure containing negative ionizers. On UV-on days, UV lights and mixing fans were turned on in the ward, and a third animal enclosure alone received ward air. TB infection in guinea pigs was defined by monthly tuberculin skin tests. All guinea pigs underwent autopsy to test for TB disease, defined by characteristic autopsy changes or by the culture of *Mycobacterium tuberculosis* from organs. 35% (106/304) of guinea pigs in the control group developed TB infection, and this was reduced to 14% (43/303) by ionizers, and to 9.5% (29/307) by UV lights (both $p < 0.0001$ compared with the control group). TB disease was confirmed in 8.6% (26/304) of control group animals, and this was reduced to 4.3% (13/303) by ionizers, and to 3.6% (11/307) by UV lights (both $p < 0.03$ compared with the control group). Time-to-event analysis demonstrated that TB infection was prevented by ionizers (log-rank 27; $p < 0.0001$) and by UV lights (log-rank 46; $p < 0.0001$). Time-to-event analysis also demonstrated that TB disease was

prevented by ionizers (log-rank 3.7; p =0.055) and by UV lights (log-rank 5.4; p=0.02). An alternative analysis using an airborne infection model demonstrated that ionizers prevented 60% of TB infection and 51% of TB disease, and that UV lights prevented 70% of TB infection and 54% of TB disease. In all analysis strategies, UV lights tended to be more protective than ionizers. In conclusion, upper-room UV lights and negative air ionization each prevented most airborne TB transmission detectable by guinea pig air sampling. Provided there is adequate mixing of room air, upper-room UV light is an effective, low-cost intervention for use in TB infection control in high-risk clinical settings. **Editors' note: Using the guinea pig air sampling model of the 1950s to advance further their DNA fingerprinting study which showed that 8.5% of 118 TB patients were responsible for 98.9% of the guinea pig infections (see issue 59 of *HIV This Week*), these authors turned their attention to preventing TB transmission. This is the first controlled evaluation assessing the effects on airborne TB transmission in a clinical setting of upper-room ultraviolet (UV) light that kills *M. tuberculosis* and negative ionization which gives airborne particles a charge that makes them stick to surfaces. Despite the high humidity of Lima (70 to 90%) which would affect UV germicidal efficacy, upper-room UV light had a marked effect reducing both TB infection (70%) and disease (54%). Although these are guinea pig studies, the evidence for this environmental control measure is strong. Upper-room UV lighting is relatively low cost compared to mechanical ventilation and should be expertly installed now in all waiting rooms, out-patient and emergency departments, and antiretroviral treatment facilities where undiagnosed and untreated TB patients are likely to be found. Designing simple UV fixtures for low-resource settings will facilitate scale-up further.**

LoBue P. Extensively drug-resistant tuberculosis. *Curr Opin Infect Dis.* 2009;22(2):167-73.

The purpose of this review was to describe the origin, epidemiology, diagnosis, treatment, prevention, and control of extensively drug-resistant tuberculosis (XDR TB). XDR TB is defined as the occurrence of TB in persons whose *Mycobacterium tuberculosis* isolates are resistant to isoniazid and rifampin and to any fluoroquinolone and at least one of three injectable second-line drugs (i.e., amikacin, kanamycin, or capreomycin). As of June 2008, XDR TB has been found in 49 countries including the United States. It generally takes several weeks to detect XDR TB using conventional culture-based methods, although some progress is being made in developing rapid molecular tests. Treatment for XDR TB is difficult, usually requiring at least 18-24 months of four to six second-line anti-TB drugs. Treatment success rates are generally 30-50%, with very poor outcomes in HIV-infected patients. Management of contacts to infectious XDR TB patients is complicated by the lack of a proven effective treatment for XDR latent tuberculosis infection. XDR TB is an emerging global health threat. The disease is difficult and expensive to diagnose and treat, and outcomes are frequently poor. New rapid diagnostic tests and new classes of anti-TB drugs are needed to successfully combat this global problem. **Editors' note: Following the death in 2006 in KwaZulu Natal of 52 of 53 patients diagnosed with XDR-TB (median survival of 16 days and 85% having acquired resistant TB rather than having developed it while under treatment), consultations were held, the definition of XDR-TB was changed, and WHO established a Global Task Force on XDR-TB. In 2007, WHO produced an eight-objective global response plan for MDR- and XDR-TB and published in 2008 its first resistance report to include XDR-TB. XDR-TB is most common in terms of absolute numbers in Eastern Europe and the former Soviet Republics of**

Central Asia. Given that MDR-TB is estimated to have increased from 270,000 cases in 2000 to 490,000 cases in 2006 and XDR-TB is estimated to represent approximately 7% of these, XDR-TB is deemed to be on the rise. The growing problem of anti-TB drug resistance and the high prevalence of HIV among TB patients in certain regions, particularly in sub-Saharan Africa, underscore the urgency of developing new TB resistance testing tools and new anti-TB treatments.

4. *People living with HIV*

Dolan Looby SE, Collins M, Lee H, Grinspoon S. Effects of long-term testosterone administration in HIV-infected women: a randomized, placebo-controlled trial. *AIDS*. 2009 Mar 12. [Epub ahead of print]

Androgen deficiency is common in HIV-infected women. Dolan Looby and colleagues investigated the long-term effects of transdermal testosterone on body composition, bone mineral density, quality of life, and safety. Twenty-five HIV-infected women with free testosterone below the median (≤ 3 pg/ml) of the female normal range were randomized to receive transdermal testosterone (300 μ g twice weekly) or identical placebo over 18 months. Women demonstrated low androgen levels (1.3 \pm 0.1 pg/ml) with relatively low weight (22.8 \pm 0.6 kg/m) and low bone mineral density (-0.61 \pm 0.17 SD hip T score) at baseline. No statistically significant differences were seen between the groups at baseline. The discontinuation rate was 16% and did not differ between treatment groups (P = 0.24). Free testosterone by equilibrium dialysis increased over 18 months (7.9 \pm 1.8 vs. 0.3 \pm 0.4 pg/ml; P = 0.002, testosterone vs. placebo). Testosterone was well tolerated and did not affect lipids, liver, or safety indices. Lean mass (1.8 \pm 0.5 vs. 0.8 \pm 0.9 kg; P = 0.04) and BMI (1.6 \pm 0.4 vs. 0.8 \pm 0.6 kg/m; P = 0.03, testosterone vs. placebo) increased in response to testosterone, whereas fat mass remained unchanged. Testosterone increased bone mineral density at the hip (0.01 \pm 0.01 vs. -0.01 \pm 0.01 g/cm; P = 0.02) and trochanter (0.01 \pm 0.01 vs. -0.02 \pm 0.01 g/cm; P = 0.01, testosterone vs. placebo). Testosterone significantly improved depression indices (-6.8 \pm 2.2 vs. -1.9 \pm 3.1; P = 0.02) and problems affecting sexual function (-1.8 \pm 0.8 vs. 0.5 \pm 0.5; P = 0.01, testosterone vs. placebo). Long-term testosterone administration was well tolerated in HIV-infected women and resulted in significant improvements in body composition, bone mineral density, and quality of life indices. Further evaluation of the safety and efficacy of testosterone use among HIV-infected women is warranted. **Editors' note: Androgen deficiency is highly prevalent among women living with HIV and is associated with reduced lean body mass, bone mineral density, and quality of life. Whereas treatment is routine in HIV-positive men with low testosterone levels, no treatment strategies exist for women with similar problems. This is the first long-term (18 months) randomised controlled trial in HIV-positive women of the effects of testosterone administered via a transdermal patch versus a control patch. Because it reveals very encouraging effects on bone mineral density, body composition, and quality of life without signs of virilisation, further studies of long-term treatment with testosterone for women living with HIV should proceed to see if these encouraging findings are confirmed.**

Franco-Paredes C, Hidron A, Tellez I, Lesesne J, Del Rio C. HIV Infection and Travel: Pretravel Recommendations and Health-Related Risks. *Top HIV Med*. 2009;17(1):2-11.

In the current era of globalization and ease of air travel combined with the increased survival attained since the advent of potent antiretroviral therapy, HIV-infected individuals are travelling to remote and resource-limited areas of the world. Travel-related health risks

in a patient with HIV depend on the patient's immune status, destination, travel itinerary, and type of travel. HIV-infected patients with a CD4+ count of 200 cells/mm³ or lower, particularly those who are treatment-naïve and newly diagnosed, are at increased risk of complications when travelling to resource-poor settings. These increased risks include those of acquiring gastrointestinal, respiratory, and endemic tropical infectious diseases. Individuals with a CD4+ count higher than 200 cells/mm³ (whether receiving antiretroviral treatment or not) are considered to have limited immune deficiency for the purpose of travel-related recommendations; in general, they may safely receive most recommended and required vaccines. Pretravel consultation before departure is crucial to address strategies to protect against vaccine-preventable diseases (routine, recommended, and required vaccinations); vector-borne diseases, particularly malaria; gastrointestinal infections; and sexually transmitted diseases. HIV-infected travellers who are ill, particularly those with fever, should undergo an immediate medical evaluation to rule out the possibility of a life-threatening infectious disease such as malaria. **Editors' note: This excellent review should be required reading for all UN staff living with HIV who travel internationally or who live in resource-constrained settings. It compiles current knowledge on the use of live attenuated and inactivated vaccines by CD4+ count and provides practical advice. This includes delaying travel until 3 months after starting antiretroviral treatment to avoid immune reconstitution syndromes during travel, keeping medication with its official documentation in hand luggage with a back-up supply in checked luggage, hand hygiene with water and soap or alcohol-based solutions, knowing about potential protease inhibitor drug interactions with malaria treatment, careful attention to water and food safety to avoid enteric infections, adherence to safer sex strategies, and the importance of prompt evaluation of fever while travelling or on return.**

5. Treatment adherence

Nachega JB, Hislop M, Nguyen H, Dowdy DW, Chaisson RE, Regensberg L, Cotton M, Maartens G. Antiretroviral Therapy Adherence, Virologic and Immunologic Outcomes in Adolescents Compared With Adults in Southern Africa. *J Acquir Immune Defic Syndr.* 2009 Mar 11. [Epub ahead of print]

Nachega and colleagues aimed to determine adherence to and effectiveness of antiretroviral therapy in adolescents vs. adults in southern Africa in an observational cohort study originating from Aid for AIDS, a private sector disease management program in southern Africa. Adolescents (age 11-19 years; n = 154) and adults (n = 7622) initiating antiretroviral treatment between 1999 and 2006 and having a viral load measurement within 1 year after antiretroviral treatment initiation were included. The primary outcomes were virologic suppression (HIV viral load \leq 400 copies/mL), viral rebound, and CD4 T-cell count at 6, 12, 18, and 24 months after antiretroviral treatment initiation. Secondary outcome was adherence assessed by pharmacy refills at 6, 12, and 24 months. The authors used a multivariate loglinear regression and Cox proportional hazards. A significantly smaller proportion of adolescents achieved 100% adherence at each time point (adolescents: 20.7% at 6 months, 14.3% at 12 months, and 6.6% at 24 months; adults: 40.5%, 27.9%, and 20.6% at each time point, respectively; $P < 0.01$). Patients achieving 100% 12-month adherence were significantly more likely to exhibit virologic suppression at 12 months, regardless of age. However, adolescents achieving virologic suppression had significantly shorter time to viral rebound (adjusted hazard ratio 2.03; 95% confidence interval: 1.31 to 3.13; $P < 0.003$). Adolescents were less likely to experience long-term immunologic recovery despite initial

CD4 T-cell counts comparable to adults. Compared with adults, adolescents in southern Africa are less adherent to antiretroviral treatment and have lower rates of virologic suppression and immunologic recovery and a higher rate of virologic rebound after initial suppression. Studies must determine specific barriers to adherence in this population and develop appropriate interventions. **Editors' note: Both because the number of adolescents on antiretroviral treatment continues to expand and because this population is most likely to benefit from optimal adherence with longest life expectancy on optimal treatment, determining the underlying reasons for the poor adherence that increases risk of morbidity and drug resistance is urgent. This study assessed adherence and outcomes among adolescents started on antiretroviral treatment when their CD4+ counts fell to 350 cells whose parents were employed by companies participating in a private sector employer-subsidized medical insurance programme in 9 countries in southern Africa. The adolescents were less likely than were adults to be on the non-nucleoside reverse transcriptase inhibitor (NNRTI)-based regimens which can achieve viral suppression with moderate levels (70-90%) of adherence. However, this cannot fully explain why adolescents were 50% less likely to maintain perfect adherence at all time points and were 70-75% less likely to be virologically suppressed at 1 and 2 years after treatment initiation. Equivalent studies in the public sector are needed to confirm these findings and qualitative studies are needed to determine the causes and provide avenues for solutions to what must be underscored as a priority treatment programme challenge.**

Tuller DM, Bangsberg DR, Senkungu J, Ware NC, Emenyonu N, Weiser SD. Transportation Costs Impede Sustained Adherence and Access to HAART in a Clinic Population in Southwestern Uganda: A Qualitative Study. *AIDS Behav.* 2009 Mar 13. [Epub ahead of print]

The cost of transportation for monthly clinic visits has been identified as a potential barrier to antiretroviral adherence in sub-Saharan Africa and elsewhere, although there is limited data on this issue. Tuller and colleagues conducted open-ended interviews with 41 individuals living with HIV and attending a clinic in Mbarara, Uganda, to understand structural barriers to antiretroviral adherence and clinical care. Almost all respondents cited the need to locate funds for the monthly clinic visit as a constant source of stress and anxiety, and lack of money for transportation was a key factor in cases of missed doses and missed medical appointments. Participants struggled with competing demands between transport costs and other necessities such as food, housing and school fees. These findings suggest that transportation costs can compromise both antiretroviral adherence and access to care. Interventions that address this barrier will be important to ensure the success of antiretroviral programs in sub-Saharan Africa. **Editors' note: With mean per capita income in Uganda the equivalent of 25 USD per month and monthly refill visit roundtrip transport costs ranging from 0.60 to 11.75 USD, it is not surprising that serious sacrifices by patients are required in other essential arenas such as food and school fees. These findings suggest that the concept of 'access to medicine or lack thereof' rather than the concept of 'failure to adhere', reframes the problem of missed doses as one anchored in structural and financial barriers that need to be addressed by treatment programmes and communities. Many ideas come to mind for piloting such as decentralisation to deliver drugs directly to the community through drug dispensaries, primary care clinics, and home-based care, along with transport cost subsidization for those being stabilised on their regimens and for subsequent 6 monthly control visits.**

Uzochukwu BS, Onwujekwe OE, Onoka AC, Okoli C, Uguru NP, Chukwuogo OI. Determinants of non-adherence to subsidized anti-retroviral treatment in southeast Nigeria. *Health Policy Plan*. 2009 Mar 10. [Epub ahead of print]

The antiretroviral treatment programme in Nigeria is delivered through selected teaching and mission hospitals at a free/subsidized rate. The government aims to scale up antiretroviral treatment in the country. However, non-adherence to antiretroviral medication can lead to viral resistance, treatment failure, toxicities and waste of financial resources. This study examined the factors responsible for non-adherence to free/subsidized antiretroviral treatment in south-east Nigeria. The study was cross-sectional and descriptive. Information was collected from 174 patients selected by simple random sampling from the register of all patients who had been on antiretroviral therapy for at least 12 months at the beginning of the study period. Patients were identified during their clinic visits. Information on their socio-demographic profile, antiretroviral treatment and determinants of non-adherence to antiretroviral treatment was obtained from those who gave consent, using pre-tested interviewer-administered questionnaires. All patients clearly understood the need to take antiretroviral drugs throughout their lives, and what the costs entailed. They understood the need for periodic testing, the probability that complications would develop, cost of transportation to treatment site and the daily treatment regimen. Seventy-five per cent of respondents were not adhering fully to their drug regimen; the mean number of days that respondents had been off drugs was 3.57 days the preceding month. Reasons for non-adherence included: physical discomfort (side effects); non-availability of drugs at treatment site; forgetting to carry drugs during the day; fear of social rejection; treatment being a reminder of HIV status; and selling of own drugs to those unable to enrol in the projects. Being female, under 35 years, single, and having higher educational status were significantly associated with non-adherence. It is important that policy makers and programme managers address the factors responsible for non-adherence when scaling up subsidized ARV treatment in Nigeria and other parts of sub-Saharan Africa. **Editors' note: With 74 treatment sites around the country in 2006 and ambitious treatment targets, Nigeria achieved only 15% access to treatment by the end of 2006 for those in need to treatment. Non-availability of drugs at the treatment centre (classic stock-outs) and side effects are the top two reasons for non-adherence in this study in Enugu State in southeastern Nigeria obtained using semi-structured questionnaires. Improved supply chain management, bimonthly rather than monthly dispensing to reduce transportation costs, and community/family/patient education about managing side effects and actively supporting adherence are some more obvious solutions.**

6. *Prevention of mother-to-child transmission*

Pai NP, Klein MB. Rapid testing at labour and delivery to prevent mother-to-child HIV transmission in developing settings: issues and challenges. *Womens Health (Lond Engl)*. 2009;5(1):55-62.

Worldwide, approximately 2.5 million children (95% CI: 2.2-2.6) are living with HIV infection. In 2007 alone, approximately 420,000 children (95%CI:350,000-540,000) were newly infected with HIV - a vast majority of these infections were acquired through maternal-foetal transmission. Many of these infections could have been reduced by timely diagnosis and the delivery of interventions aimed at preventing mother-to-child HIV transmission. This perspective examines the attitudes preventing women from accessing HIV testing early on

during pregnancy and the issues and challenges that remain in the institutionalization of interventions to prevent mother-to-child HIV transmission at labour and delivery. Socio-cultural and economic factors prevent women from accessing testing at an opportune time during pregnancy. In addition, a lack of adequate infrastructure often prevents timely delivery of interventions to those who access testing at the last minute (i.e., during labour and delivery). In the wake of a paediatric HIV epidemic and the need for lifelong provision of antiretroviral therapy to infected children, a simple strategy for provision of round-the-clock rapid testing and counselling services in the labour rooms may be cost saving to the healthcare systems worldwide. **Editors' note: Although studies of programmes of point-of-care rapid HIV testing in labour and delivery have been conducted around the world, the need for additional infrastructure resources, such as round-the-clock counsellors and user friendly and accurate rapid tests, has been an impediment to wider implementation. With only 33% of women needing antiretroviral prophylaxis in pregnancy worldwide actually able to access it, innovations are needed to improve coverage. Labour and delivery are not times conducive to reflection on the personal advantages and disadvantages of knowledge of serostatus but two-stage counselling (short prepartum and extended postpartum), attention to privacy and confidentiality, timely confirmation of results to reduce false-positives and false-negatives, and community-based education engaging partners and highlighting the importance of preventing HIV transmission to infants could identify more babies in need of intrapartum and post-exposure prophylaxis and more mothers needing tailored infant feeding counselling in addition to evaluation for antiretroviral treatment, and care and support.**

Lazarus R, Struthers H, Violari A. Hopes, fears, knowledge and misunderstandings: responses of HIV-positive mothers to early knowledge of the status of their baby. *AIDS Care*. 2009;21(3):329-34.

Little is known about how HIV-positive mothers experience and react to knowing the HIV status of their baby as diagnosed by the polymerase chain reaction (PCR) test at 4-6 weeks. This qualitative study drew on interviews with 20 mothers of HIV-negative and 18 mothers of HIV-positive babies after receiving their baby's PCR results. Thematic analysis combined exploration of themes that appeared significant to the participants and those relevant to health care. Amongst the themes identified were the following: The period before getting the results involved active mental preparation and was emotionally stressful. Most women accepted the results, but some had doubts about their reliability. Mothers of HIV-negative babies were relieved, but mothers of HIV-positive babies were generally very distressed and expressed a sense of responsibility and guilt. Both groups of mothers had similar hopes for the future of their babies, but the timelines of mothers of HIV-positive babies tended to be shorter. Most women experienced significant levels of stress, but were able to call on support networks and use various individual coping mechanisms to manage their stress. Most women were formula feeding their babies, but regretted not being able to breastfeed. Many women had not planned their current baby and most did not intend to have more children, but many of the latter had not taken active steps to prevent further pregnancy. The findings provide pointers to shortcomings in health worker communication and suggest that more effective communication should take account of normative community views and be more closely attuned to the changing needs and experiences of HIV-positive mothers. **Editors' note: This study in the urban township of Soweto in Johannesburg, South Africa supports the notion that HIV-positive mothers prefer learning their babies' status early**

at 4 to 6 weeks rather than waiting for 12 or more months until maternal antibodies disappear. The need for improvement in health care worker communication is evident from the fact that most of the mothers of infected children planned to replacement feed although breastfeeding offers more benefits to HIV-positive infants than risks of re-infection. As well, although most women said this baby had been unplanned and they would not want to have another, health care workers concentrated on condoms as means of reducing risk of transmission to partners, rather than as contraceptives, and some discouraged sterilisation as a more permanent fertility control option. This is a good example of how data collected using qualitative, in-depth interviews guided by a set of open-ended questions posed to end-users can underscore the need for training and enhanced service delivery.

7. Injecting Drug Use

Altaf A, Saleem N, Abbas S, Muzaffar R. High prevalence of HIV infection among injection drug users (IDUs) in Hyderabad and Sukkur, Pakistan. *J Pak Med Assoc.* 2009;59(3):136-40.

Altaf and colleagues aimed to estimate size of the injecting drug user population, determine the behaviours that put injecting drugs users at high-risk of HIV exposure, and assess the prevalence of HIV. As part of second generation surveillance, they investigated specific demographic and behavioural characteristics of people who inject drugs in Hyderabad and Sukkur in 2005. It was a cross sectional study. The survey was preceded by geographic mapping to determine size estimation and to define sampling procedures prior to conduct an integrated behavioural and biological survey. A sample size of at least 400 was calculated for each city. Besides calculating frequencies, chi square was used for comparing variables among HIV positive and negative injecting drug users like time elapsed as an injector, number of injections, using unsterile needles, and self perception of risk of acquiring HIV infection. A total of 800 (Hyderabad 398; Sukkur 402) questionnaires and dried blood samples were collected. The estimated number of injecting drug users in both cities was 3,225 (Hyderabad 975 and Sukkur 2250 respectively). Average age of the injectors in Hyderabad was 36.5 years and 34.6 years in Sukkur. Using unsterile injecting equipment for last injection was reported by 34 (8.5%) in Hyderabad and 135 (33.6%) in Sukkur. In both cities behaviours such as injecting drugs for more than 10 years ($p = 0.00$) and injecting four or more times in a day ($p = 0.11$) were significantly associated with HIV seropositivity. In Hyderabad the HIV seroprevalence was 25.4% (101/398) and in Sukkur it was 19.2% (77/402). In conclusion, the burden of HIV among people who inject drugs in Hyderabad and Sukkur is extremely high and can play a significant role in transmitting the infection to other vulnerable groups. **Editors' note: Fluctuations in heroin availability, purity, and price have led many of the estimated 484, 000 heroin users in Pakistan to change over to injecting rather than less cost-efficient snorting or smoking. This first reported serosurvey from Hyderabad and Sukkur in Sindh province north of Karachi reveals that over one in five injectors (defined as having injected drugs for non-therapeutic purposes in the past 6 months) in these cities already has HIV infection. There is an urgent need for an organised programme of harm reduction services in both cities to reduce the negative health, social, and economic consequences of drug use for individual injectors and the wider community.**

8. Prognosis

Willard S, Holzemer WL, Wantland DJ, Cuca YP, Kirksey KM, Portillo CJ, Corless IB, Rivero-Méndez M, Rosa ME, Nicholas PK, Hamilton MJ, Sefcik E, Kemppainen J, Canaval G, Robinson L,

Moezzi S, Human S, Arudo J, Eller LS, Bunch E, Dole PJ, Coleman C, Nokes K, Reynolds NR, Tsai YF, Maryland M, Voss J, Lindgren T. Does "asymptomatic" mean without symptoms for those living with HIV infection? *AIDS Care*. 2009;21(3):322-8.

Throughout the history of the HIV epidemic, HIV-positive patients with relatively high CD4 counts and no clinical features of opportunistic infections have been classified as "asymptomatic" by definition and treatment guidelines. This classification, however, does not take into consideration the array of symptoms that an HIV-positive person can experience long before progressing to AIDS. This short report describes two international multi-site studies conducted in 2003-2005 and 2005-2007. The results from the studies show that HIV-positive people may experience symptoms throughout the trajectory of their disease, regardless of CD4 count or classification. Providers should discuss symptoms and symptom management with their clients at all stages of the disease. **Editors' note: Both physical and psychological symptoms were reported by 'asymptomatic' people living with HIV regardless of CD4 count category or whether they were on antiretroviral medications. The twenty most frequently reported symptoms in the 33 to 60% range included fatigue (57-60%), depression, muscle aches, weakness, thirst, worry, difficulty concentrating, memory loss, dry mouth, insomnia, joint pain, diarrhoea, shortness of breath with activity, night sweats, gas/bloating, headaches, abdominal pain, and numbness/tingling of hands/fingers or feet/toes or legs (33 to 37%). Recognising both the broad variation in how patients perceive and rate their symptom experience and that many of these symptoms in HIV-positive individuals can be addressed by specific measures just as they can be in HIV-negative people, clinicians need to carefully interview their 'asymptomatic' patients for the presence of symptoms and address symptom management to improve quality of life.**

Madec Y, Szumilin E, Genevier C, Ferradini L, Balkan S, Pujades M, Fontanet A. Weight gain at 3 months of antiretroviral therapy is strongly associated with survival: evidence from two developing countries. *AIDS*. 2009;27(7):853-61.

In developing countries, access to laboratory tests remains limited, and the use of simple tools such as weight to monitor HIV-infected patients treated with antiretroviral therapy should be evaluated. Madec and colleagues conducted a cohort study of 2451 Cambodian and 2618 Kenyan adults who initiated antiretroviral therapy between 2001 and 2007. The prognostic value of weight gain at 3 months of antiretroviral therapy on 3-6 months mortality, and at 6 months on 6-12 months mortality, was investigated using Poisson regression. Mortality rates [95% confidence interval (CI)] between 3 and 6 months of antiretroviral therapy were 9.9 (7.6-12.7) and 13.5 (11.0-16.7) per 100 person-years in Cambodia and Kenya, respectively. At 3 months, among patients with initial body mass index less than or equal to 18.5 kg/m² (43% of the study population), mortality rate ratios (95% CI) were 6.3 (3.0-13.1) and 3.4 (1.4-8.3) for those with weight gain less than or equal to 5 and 5-10%, respectively, compared with those with weight gain of more than 10%. At 6 months, weight gain was also predictive of subsequent mortality: mortality rate ratio (95% CI) was 7.3 (4.0-13.3) for those with weight gain less than or equal to 5% compared with those with weight gain of more than 10%. Weight gain at 3 months is strongly associated with survival. Poor compliance or undiagnosed opportunistic infections should be investigated in patients with initial body mass index less than or equal to 18.5 and achieving weight gain less than or equal to 10%. **Editors' note: While CD4+ count and viral load remain the gold standards for monitoring patients on antiretroviral treatment, simple tools such as weight gain at 3 months can alert providers to the need to assess adherence, the presence of an**

opportunistic infection such as tuberculosis, or poor nutritional intake. Whereas overall programme performance can be measured by the proportion of patients achieving at least 10% weight gain at 6 months, the 3-month point is more critical for patient evaluation. As this study of over 5000 Cambodians and Kenyans initiating antiretroviral treatment shows, there was a 6-fold increase in risk of dying for patients with less than or equal to 5% weight gain compared to those with more than 10% weight gain at 3 months. CD4 count at treatment initiation was no longer predictive of mortality between 3 and 6 months once weight gain at 3 months was taken into account. Until antiretroviral treatment is more widely available so that patients initiate treatment at an earlier stage of infection, simple, low-cost weight monitoring will be particularly relevant.

9. Reproductive Health

Semprini AE, Hollander LH, Vucetich A, Gilling-Smith C. Infertility treatment for HIV-positive women. *Womens Health* (Lond Engl). 2008;4(4):369-82.

Thanks to antiretroviral combination therapy, HIV-infected individuals live longer, healthier lives and may wish to have children. Women with HIV can attempt to conceive naturally or through simple self-insemination to minimize the risk of horizontal HIV transmission. Assisted reproduction technology is necessary in couples with infertility, which can either be independent of HIV infection and its treatment or be associated with it. This article summarizes the latest evidence regarding the desire for a child in HIV-positive women and how HIV infection and its treatment may impact female fertility. Current data regarding access to and outcomes of assisted conception programs in HIV-positive women wishing to conceive in both high- and low-income countries are also reviewed. **Editors' note: This exhaustive review covers the evidence that women living with HIV have similar levels of intentions to be a parent as do other women, that pregnancy itself does not worsen the immunological status of HIV-positive women and is not correlated with disease progression, and that HIV-positive women experience increased tubal infertility and reduced ovarian reserve. Limiting unprotected intercourse to the day of ovulation in women who have been screened and treated for sexually transmitted infections can reduce but not eliminate the risk of horizontal transmission to the male partner. The authors favour low-cost, home-based, simple self-insemination which eliminates the risk of HIV transmission to the uninfected male partner. If after 6 cycles of self-insemination with no conception, fertility investigations should begin. Emphasising that leading professional organisations state that assisted reproductive techniques should not be denied HIV-infected couples, the authors conclude with a section on limiting the risks of HIV transmission associated with *in vitro* fertilisation - intracytoplasmic sperm injection techniques and highlighting the success of sperm-washing programmes in Europe.**

10. Basic Science

Scheid JF, Mouquet H, Feldhahn N, Seaman MS, Velinzon K, Pietzsch J, Ott RG, Anthony RM, Zebroski H, Hurley A, Phogat A, Chakrabarti B, Li Y, Connors M, Pereyra F, Walker BD, Wardemann H, Ho D, Wyatt RT, Mascola JR, Ravetch JV, Nussenzweig MC. Broad diversity of neutralizing antibodies isolated from memory B cells in HIV-infected individuals. *Nature*. 2009;458(7238):636-40.

Antibodies to conserved epitopes on the human immunodeficiency virus (HIV) surface protein gp140 can protect against infection in non-human primates, and some infected individuals show high titres of broadly neutralizing immunoglobulin (Ig)G antibodies in their serum. However, little is known about the specificity and activity of these antibodies. To characterize the memory antibody responses to HIV, Scheid and colleagues cloned 502 antibodies from HIV envelope-binding memory B cells from six HIV-infected patients with broadly neutralizing antibodies and low to intermediate viral loads. They show that in these patients, the B-cell memory response to gp140 is composed of up to 50 independent clones expressing high affinity neutralizing antibodies to the gp120 variable loops, the CD4-binding site, the co-receptor-binding site, and to a new neutralizing epitope that is in the same region of gp120 as the CD4-binding site. Thus, the IgG memory B-cell compartment in the selected group of patients with broad serum neutralizing activity to HIV is comprised of multiple clonal responses with neutralizing activity directed against several epitopes on gp120. **Editors' note: Although the possibility exists that a single highly effective antibody may produce broadly neutralizing activity in serum, to date it has not been possible to isolate such an antibody from patients or induce it by immunisation in experimental animals. These findings from a study of 6 'elite controller' patients suggest, however, that a vaccine that could copy the natural anti-HIV immune response seen in patients with broadly neutralising serological activity and elicit a combination of antibodies might also be an effective means of protection against a large number of HIV strains.**

Cao W, Jamieson BD, Hultin LE, Hultin PM, Effros RB, Detels R. Premature Aging of T cells is Associated With Faster HIV-1 Disease Progression. *J Acquir Immune Defic Syndr.* 2009;50(2):137-47.

Cao and colleagues aimed to determine if untreated HIV-1 infection and progression is associated with premature aging of memory CD8 and CD4 T cells and naive CD4 T cells. Twenty HIV-1-infected fast progressors and 40 slow progressors were included in the study, using risk set sampling. The expression of cell surface markers reflecting the differentiation stages of lymphocytes was measured using flow cytometry analyses performed on cryopreserved peripheral blood mononuclear cells. The authors found that HIV-1 disease progression is associated with a decreased CD28 median fluorescence intensity on CD4 and CD8 T cells; an increased proportion of intermediate- and late-differentiated CD8 T cells and a decreased CD31 median fluorescence intensity on naive CD4 T cells of recent thymic origin. A selective depletion of peripherally expanded naive CD4 T cells was found to be associated with HIV-1 infection but not with HIV-1 disease progression. The overall change during HIV-1 infection and progression is associated with a shift in the T-cell population toward an aged conformation, which may be further compromised by impaired renewal of the less-differentiated CD4 T-cell population. Their results suggest that HIV-1 infection induces an accelerated aging of T lymphocytes, which is associated with the clinical progression to AIDS and death. **Editors' note: This study comparing 20 fast progressors with 40 slow progressors found that HIV-1 infection itself induces premature aging of both memory T-cells and naïve CD4+ T cells. Fast progressors experience accelerated aging of lymphocytes, which display reduced replicative capacity and shortened telomeres. This overall structural change to more aged memory T-cells may be due to accelerated differentiation driven by chronic antigenic stimulation and immune activation. Possible therapeutic approaches could include physically removing aged T cells to make room for**

more functional earlier subsets and using drugs to enhance telomerase activity to slow the shortening of telomere length.

11. Positive prevention

Gilliam PP, Straub DM. Prevention with positives: a review of published research, 1998-2008. *J Assoc Nurses AIDS Care*. 2009 Mar-Apr;20(2):92-109.

HIV prevention education and counselling efforts have historically been directed toward those individuals considered at risk for exposure to HIV and assumed to be uninfected with HIV. In the late 1990s, prevention efforts began to include individuals who were HIV-infected. In 2003, the United States Centers for Disease Control and Prevention recommended that HIV prevention be incorporated into the medical care of persons living with HIV. This domain of HIV prevention work is known as prevention with positives or positive prevention, and research within this domain has been ongoing for a decade. This article provides a review of the scientific evidence within the prevention with positives domain from 1998 to 2008. A discussion is provided regarding early descriptive and formative studies as well as more recent and ongoing intervention trials specifically designed for persons living with HIV. A summary of current knowledge, a description of ongoing research, and gaps in knowledge are identified. Topics for future research are suggested.

Editors' note: This is a relatively new area of endeavour and therefore there are only preliminary results available for 11 of the 17 intervention trials conducted in the United States. The trials are grouped into two distinct categories: interventions delivered in the community in multiple sessions facilitated by professionals other than medical care providers and interventions incorporated into the medical care of people living with HIV using brief counselling techniques, delivered within the clinic setting, and including the patient's care provider in the delivery of the prevention message. All use a theory grounded in behavioural change with the premise that HIV transmission is a behavioural phenomenon (e.g. Bandura, Prochaska and DiClemente, Fisher and Fisher, etc) with only one theoretical foundation focused on a subpopulation, based on a theory of gender and power (Wingood and DiClemente). As results become available, cost analyses will help in deciding whether the brief intervention delivered in the context of a routine medical visit wins out.

Copenhaver M, Chowdhury S, Altice FL. Adaptation of an Evidence-Based Intervention Targeting HIV-Infected Prisoners Transitioning to the Community: The Process and Outcome of Formative Research for the Positive Living Using Safety (PLUS) Intervention. *AIDS Patient Care STDS*. 2009 Mar 4. [Epub ahead of print]

No evidence-based interventions have been designed for implementation during the critical period when HIV-infected prisoners are being transitioned from prison to the community. Copenhaver and colleagues therefore conducted formative research aimed at systematically selecting and adapting an evidence-based intervention that integrates HIV risk reduction and adherence to antiretroviral therapy to implement among HIV-infected prisoners transitioning back to the community. Their formative research involved a critical examination of established evidence-based interventions and associated published reports complemented by data elicited through structured interviews with key stakeholders in community and correctional settings and members of the target population. Between September 2006 and February 2007, structured one-on-one interviews were conducted with key stakeholders in the target organizations (n = 19) and with members of the target population (n = 26) in Hartford and New Haven, Connecticut. Based on the formative research, the authors

abbreviated and adapted the Holistic Health Recovery Program targeting people living with HIV (HHRP+), an evidence-based intervention, to consist of four 45-minute sessions that cover a range of prespecified topics so that participants may individually apply intervention content as needed to their own HIV risk profile and antiretroviral adherence issues. The evidence-based intervention was adapted so that it could be provided in an individual or group format and delivered in either consecutive or weekly sessions and so that it could be provided within the prison system and delivered just prior to release, or in a community-based setting where it could be delivered immediately after release. This study provides a comprehensive exemplar of the process of selecting and adapting an evidence-based intervention taking into account both empirical evidence and input from target organization stakeholders and target population members in real-world settings where high-risk populations are concentrated. **Editors' note: With as many as 25% of HIV-infected people in the United States passing through the correctional system each year, primarily due to policies incarcerating drug users, opportunities for improving the health of this 'captive' audience are real. Given evidence of a strong positive association between the length of incarceration of HIV-positive people and their health and well-being, the challenge is how to maintain these HIV-related health benefits when people leave the highly structured prison environment. This formative study began with an extensive literature review of interventions for people living with HIV with a history of drug use. Then prisoners with this profile and treatment providers in correctional and community-based treatment settings were enlisted to determine what intervention content would be most relevant, what design characteristics (modality and duration) would be most feasible, and what mechanisms of referral to the programme would be most appropriate. The results take into account the real world needs of the intended participants as well as the constraints of the prison and community settings where they are found. Now we await the outcome of the programme itself.**

That was *HIV this week*, signing off.

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