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HIV This Week: what scientific journals said

Welcome to issue fifty-two of ***HIV This Week***! In this issue, we cover **gender** (transgender women more at risk than transgender men in the USA; only part of the way there: integrating sexual and reproductive health and rights into antiretroviral treatment programmes in Cape town), **civil society responses** (lessons learned from 25 years of HIV in Europe), **young people** (parent-adolescent communication not fostered in a randomised controlled trial (RCT) in the Bahamas), **preventing sexual transmission** (coping skills building reduces transmission risk behaviour among people living with HIV who were sexually abused as children), **infant diagnosis** (promising results with a dried blood spot polymerase chain reaction test in China; dried blood spot p24 antigen ELISA in South Africa brings early diagnosis in infants one step closer), **human resources for health** (task shifting in the limelight), **basic science** (firing up the troops for an HIV vaccine; how do vaccines work and how far do we have to go for an HIV one; genetic therapies against HIV: the plot thickens!), **injecting drug use** (high time to integrate and co-locate services), **country responses** (from Chuuk State, Micronesia: a creative HIV prevention strategy on remote islands), **prevention programme design** (let's get bundling for synergistic gain!), **treatment and care** (case management for very depressed Torontonians living with HIV saves money and improves quality of life), **paediatric treatment and care** (rethinking vaccine schedules for children born to HIV-positive mothers in central Africa; why caregivers are so key for adherence to antiretroviral therapy in Brazilian children; Burkitt's lymphoma on the rise in eastern Africa), **structural determinants and vulnerability** (nearly 13% of South African educators are living with HIV: what can be done to prevent further HIV acquisition?; sex work linked to food insecurity in Nigeria is set to intensify as the global food crisis deepens), and **stigma** (layered stigmatisation in Hong Kong will require changes in attitudes to vulnerable groups).

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1. Gender

Herbst JH, Jacobs ED, Finlayson TJ, McKleroy VS, Neumann MS, Crepaz N; for the HIV/AIDS Prevention Research Synthesis Team. Estimating HIV Prevalence and Risk Behaviors of Transgender Persons in the United States: A Systematic Review. *AIDS Behav* 2007; 12(1):1-17.

Transgender populations in the United States have been affected by the HIV epidemic. This systematic review estimates the prevalence of HIV infection and risk behaviours of transgender persons. Comprehensive searches of the US-based HIV behavioural prevention literature identified 29 studies focusing on male-to-female transgender women; five of these studies also reported data on female-to-male transgender men. Using meta-analytic approaches, prevalence rates were estimated by synthesizing weighted means. Meta-analytic findings indicated that 27.7% (95% confidence interval [CI], 24.8-30.6%) of male-to-female transgender women tested positive for HIV infection (four studies), while 11.8% (95% CI, 10.5-13.2%) of male-to-female transgender women self-reported being HIV-seropositive (18 studies). Higher HIV infection rates were found among African-American male-to-female transgender women regardless of assessment method (56.3% test result; 30.8% self-report). Large percentages of male-to-female transgender women (range, 27-48%) reported engaging in risky behaviours (e.g., unprotected receptive anal intercourse, multiple casual partners, sex work). HIV prevalence and risk behaviours were low among female-to-male transgender men. Contextual factors potentially related to increased HIV risk include mental health concerns, physical abuse, social isolation, economic marginalization, and unmet transgender-specific healthcare needs. Additional research is needed to explain the causes of HIV risk behaviour of transgender persons. These findings should be considered when developing and adapting prevention interventions for transgender populations. **Editors' note: This systematic review highlights marked differences in HIV prevalence by self-report versus actual HIV testing and in HIV prevalence and risk behaviour between male-to-female transgender women and female-to-male transgender men. In the four studies that included HIV testing, HIV prevalence in transgender women exceeded that of men who have sex with men in 5 US cities and was highest among African-American transgender women. Prevention programmes encouraging transgender persons to practice safer sex behaviours within different types of sexual relationships risk failure if they do not address the individual, interpersonal, and structural/societal contexts influencing their sexual and injecting behaviour.**

Myer L, Rebe K, Morroni C. Missed opportunities to address reproductive health care needs among HIV-infected women in antiretroviral therapy programmes. *Trop Med Int Health*. 2007; 12(12):1484-9.

Myer and colleagues investigate the delivery of reproductive health care services in an antiretroviral therapy programme in Cape Town, South Africa. A cross-sectional survey was conducted among 227 consecutive women attending a hospital-based antiretroviral therapy outpatient service who had been on antiretroviral therapy for at least one month. Semi-structured interviews investigating reproductive health issues and services received were conducted in participants' home language by a trained interviewer. Sixty-seven per cent of the women were younger than 30 years and 75% were sexually active. The use of both condoms (70%) and hormonal contraceptives (31%) decreased with age, while the prevalence of sterilization (13%) increased with age. Few women knew about emergency contraception (7%) or termination of pregnancy (13%). Approximately 45% of women had had a Papanicolaou

smear, and this was constant across all age groups. One in 10 women had experienced verbal or physical abuse by an intimate partner since their HIV diagnosis. More than 80% of women had discussed the use of condoms and other forms of contraception with a health care provider since their HIV diagnosis, but less than 5% had discussed emergency contraception or termination of pregnancy, and no woman had discussed issues of partner violence. These data delineate the large unmet need for reproductive health services among HIV-infected women receiving antiretroviral therapy in this setting. While issues related to condom and contraceptive use are relatively well addressed, reproductive health services related to unintended pregnancy and partner violence appear to be neglected. The integration of a broad range of reproductive health services into antiretroviral therapy programmes requires urgent attention in both research and policy-making circles. **Editors' note: Systematic investigations of the reproductive health needs of women on antiretroviral treatment in sub-Saharan Africa are rare. Most antiretroviral programmes focus on condoms and sexual risk reduction counselling to prevent ongoing sexual transmission and on contraception to prevent unwanted pregnancies and danger to the foetus posed by some antiretroviral drugs. Often they do not address comprehensive reproductive health care needs including emergency contraception, termination of pregnancy, gender-based violence, and screening to prevent cervical cancer, which is itself an AIDS-defining condition. Creating one-stop services by integrating reproductive health fully into antiretroviral programmes supports the sexual and reproductive health and rights of women living with HIV. Such integration is urgently needed both in urban settings where it may be easier to accomplish and in rural settings across sub-Saharan Africa.**

2. Civil society responses

Atun RA, McKee M, Coker R, Gurol-Urganci I. Health systems' responses to 25 years of HIV in Europe: Inequities persist and challenges remain. *Health Policy*. 2008; 86(2-3):181-94.

Europe is currently experiencing the fastest rate of growth of HIV of any region of the world. An analysis of policy and health system responses to the HIV epidemic in Europe and central Asia (hereafter referred to as Europe) over the last 25 years reveals considerable heterogeneity. In general, while noting hazards of broad generalisations and the differences that exist across countries in a particular grouping, effective policies to control HIV have been implemented more widely in western than in central and Eastern Europe. However, the evidence suggests persistence of inequalities in access to preventive and treatment services, with those at highest risk, such as sex workers, prisoners, injecting drug users, and migrants often particularly disadvantaged, despite many targeted programmes. Responses in individual countries, especially in the early stages of the epidemic, were influenced by specific cultural and political factors. Strong leadership and active involvement by civil society organisations emerge as important factors for success but also a limiting factor to the response observed in Eastern Europe, where civil society or Non-Governmental Organization culture is weak as compared to Western Europe. Scaling up of effective responses in many countries in Eastern Europe will be challenging. Increased financial resources will have to be accompanied by broader changes to health system organization with greater involvement of civil society in planning and delivery of client-focused services. **Editors' note: This desk review combined countries with differing socioeconomic, cultural, and health systems characteristics into four broad groupings: Western, Central, Eastern Europe, and Central Asia. The multi-sectored, client-focused interventions of Western Europe are integrated into**

mainstream health systems offering broad coverage, but inequities persist for marginalized people. In the countries of Eastern Europe facing HIV, IDU, STI, and TB epidemics, new resources directed at programmatic interventions alone will not be effective in addressing either the HIV epidemic or the persistent inequities that exacerbate it, nor will they be sustainable. The design and implementation of multifaceted and multi-sectored programmes must be shaped by the local, political, economic, social, and legal contexts and serve to strengthen health systems, surveillance, monitoring and evaluation, and civil society engagement.

3. Young people

Deveaux L, Stanton B, Lunn S, Cottrell L, Yu S, Brathwaite N, Li X, Liu H, Marshall S, Harris C. Reduction in human immunodeficiency virus risk among youth in developing countries. *Arch Pediatr Adolesc Med.* 2007; 161(12):1130-9.

Deveaux and colleagues address the 6-month efficacy of a human immunodeficiency virus (HIV) prevention intervention targeted to youth and delivered with and without a parental monitoring intervention in a developing country (the Bahamas). The authors conduct a randomized, controlled, 3-cell intervention trial with a 6-month postintervention follow-up in a total of 1282 Bahamian sixth-grade students (and 1175 parents) in 15 elementary schools in the Bahamas. Youth and parents were randomized at the level of the school to receive the following interventions: (1) Focus on Youth in the Caribbean (FOYC) plus Caribbean Informed Parents and Children Together (CImPACT), (2) FOYC plus an attention control for parents (Goal for It [GFI]), or (3) an attention control for the youth (Wonderous Wetlands [WW]) plus the GFI. The 10-session FOYC or WW curriculum was delivered as part of the elementary school curriculum. The GFI or CImPACT was delivered to parents in the evenings or on weekends. Risk and protective knowledge, condom use skills, perceptions, interventions, and self-reported behaviours were measured. Compared with the WW, the FOYC significantly increased knowledge, condom use skills, protective perceptions, and intentions to engage in safer behaviours. Among youth, no differences were found in knowledge or condom use skills based on parent intervention; among parents, those receiving the CImPACT demonstrated superior condom use skills after the intervention. In conclusion, protective knowledge, skills, perceptions, and intentions of youth from one developing country can be significantly improved by youth intervention delivered through the schools. Longer follow-up is needed to determine if risk behaviours will be reduced and how long protective results will be sustained. **Editors' note: It is not surprising that a 10-chapter theory-based school-based HIV intervention emphasising skill development, practice in negotiation, and communication/decision-making had greater effects on knowledge and intentions to practice sexual protective behaviour than a 10-chapter curriculum emphasising the importance of water conservation, wild life, and other natural resources in the Bahamas. What is surprising is that there was no difference in adolescent scores when their parents participated in ImPACT, a parental monitoring and communication intervention that had been effective in the USA in reducing adolescent HIV risk behaviours when combined with a similar adolescent risk reduction intervention, compared to a control intervention for parents (a 20 minute video about career goals). The most likely explanation may be that ImPACT, which included a condom demonstration, was modified for the Bahamas for delivery only to parents and not to parents and youth together. The opportunity was missed to foster the parental-adolescent communication that can make all the difference.**

4. Preventing sexual transmission

Sikkema KJ, Wilson PA, Hansen NB, Kochman A, Neufeld S, Ghebremichael MS, Kershaw T. Effects of a coping intervention on transmission risk behavior among people living with HIV/AIDS and a history of childhood sexual abuse. *J Acquir Immune Defic Syndr*. 2008; 47(4):506-13.

Sikkema and colleagues examine the effect of a 15-session coping group intervention compared with a 15-session therapeutic support group intervention among HIV-positive men and women with a history of childhood sexual abuse on sexual transmission risk behaviour. In a randomized controlled behavioural intervention trial with 12-month follow-up, a diverse sample of 247 HIV-positive men and women with histories of childhood sexual abuse was randomized to 1 of 2 time-matched group intervention conditions. Sexual behaviour was assessed at baseline; immediately after the intervention; and at 4-, 8-, and 12-month follow up periods (5 assessments). Changes in frequency of unprotected anal and vaginal intercourse by intervention condition were examined using generalized linear mixed models for all partners, and specifically for HIV-negative or serostatus unknown partners. Participants in the HIV and trauma coping intervention condition decreased their frequency of unprotected sexual intercourse more than participants in the support intervention condition for all partners (P < 0.001; d = 0.38, 0.32, and 0.38 at the 4-, 8-, and 12-month follow-up periods, respectively) and for HIV-negative and serostatus unknown partners (P < 0.001; d = 0.48, 0.39, and 0.04 at the 4-, 8-, and 12-month follow-up periods, respectively). The authors conclude that a group intervention to address coping with HIV and childhood sexual abuse can be effective in reducing transmission risk behaviour among HIV-positive men and women with histories of sexual trauma. **Editors' note: From one-third to two-thirds of people living with HIV in the USA report a history of having been sexually abused as children, more than double the estimated rates in the general population. The association between childhood sexual abuse and sexual risk behaviours is well documented. The participants randomised to the coping group intervention benefited from adaptive coping skills building for confronting the combined stress and emotional consequences of child sexual abuse and HIV. Focusing on psychological adjustment and development of adaptive coping skills had a significantly greater effect on safer sex practices than a therapeutic support group and probably had similar unmeasured effects on coping in other areas of life.**

5. Infant diagnosis

Zhang Q, Wang L, Jiang Y, Fang L, Pan P, Gong S, Yao J, Tang YW, Vermund SH, Jia Y. Early infant HIV-1 diagnosis suitable for resource-limited settings with multiple circulating subtypes: Nested, 3-monoplex DNA PCR on dried blood spots. *J Clin Microbiol*. 2007; 46(2):721-6.

Early infant diagnosis of HIV-1 infection is complicated by the persistence of maternal antibodies and by diverse HIV-1 subtypes. Zhang and colleagues developed a nested, 3-monoplex HIV-1 DNA polymerase chain reaction (N3M-PCR) assay to detect diverse HIV-1 subtypes in infants born to infected mothers. They optimized the test for use with dried blood spot samples for ease of storage and transport from rural China to central laboratories. Six pairs of primers were designed targeting env, gag, and pol genomes run in three reactions with an analytical sensitivity of 10 copies DNA per reaction to cover nine HIV-1 subtypes A, B, C, D, F, G, CRF01_AE, CRF08_BC, and CRF07_BC. Assay performance was evaluated on 347 dried blood spot specimens from 151 exposed infants in four diverse provinces of China with multiple circulating subtypes. Results were compared with HIV

antibody enzyme immunoassay and Western blot confirmation in the infants at ≥ 18 months of age, or convincing clinical and epidemiologic data for deceased infants. Sensitivity of the N3M-PCR assay was 30.0% (3/10) for infants at 48 hours after birth, 91.7% (11/12) at 1-2 months, and 93.7% (15/16) at 3-6 months of age. Specificity was 100% (94/94) at all three time points. The polymerase chain reaction reproducibility in the three DNA regions was 100% for samples at 48 hours after birth, 96.7% at 1-2 months, and 100% at 3-6 months of age. The HIV-1 DNA N3M-PCR assay on dried blood spots offers a simple and affordable approach for early infant HIV-1 diagnosis in regions with diverse HIV-1 circulating subtypes.

Editors' note: The numbers of samples tested in this study in China are small but the results are very encouraging. This polymerase chain reaction (PCR) test is detecting the virus, not antibody, and its performance is judged against the presence of antibodies after 18 months of age. Test sensitivity is good by one month when the test is missing up to 10% of infected infants and test specificity is excellent (no false positive results) from 48 hours of life on. Dried blood spots (DBS) require minimal storage facilities because they are stable at room temperature for prolonged periods and can be safely and easily shipped for centralised testing with economies of scale. As for the DBS-ELISA of Patton et al (below), further testing of the DBS-PCR for infant diagnosis is now needed on a larger scale.

Patton JC, Coovadia AH, Meyers TM, Sherman GG. Evaluation of the Ultrasensitive Human Immunodeficiency Virus (HIV) -1 p24 Antigen Assay on Dried Blood Spots (DBS) for Infant Diagnosis. *Clin Vaccine Immunol* 2007; 15(2):388-91.

The diagnostic accuracy of the modified p24 Ag assay on paediatric dried blood spots was evaluated. Samples analyzed within 6 weeks of collection yielded no false positive results (specificity 100%) and few false negative results (sensitivity 96.5%-98.3%). Laboratory services with limited resources should assess this option for routine infant diagnosis.

Editors' note: In this South African study, dried blood spot specimens from 147 six-week old babies born to HIV-seropositive mothers and 99 children known to be infected (median age 20 months) were tested with good sensitivity and excellent specificity. Dried blood spots were obtained from capillary blood obtained by heel stick. The test was an ultra sensitive 24 antigen ELISA and specimens were collected on two types of filter paper. Storage with a desiccant conserved test sensitivity. As with the DBS-PCR of Zhang et al (above), testing should proceed in other settings with larger numbers to validate these findings.

6. Human resources for health

Samb B, Celletti F, Holloway J, Van Damme W, De Cock KM, Dybul M. Rapid expansion of the health workforce in response to the HIV epidemic. *N Engl J Med*. 2007; 357(24):2510-4.

The World Health Organization (WHO) estimates that there is now a global deficit of more than 4 million trained health workers. The shortages in health workers are critical in 57 countries, mostly in sub-Saharan Africa and parts of Asia. The situation is further exacerbated by the direct effect of the human immunodeficiency virus (HIV) on health workers in resource-constrained countries in which the disease is epidemic. Poor working conditions and low pay conspire with the risks of occupational transmission and the stress of working in communities devastated by the HIV epidemic to drive up rates of attrition. In countries with the highest rate of HIV, leading causes of attrition are the morbidity and mortality caused by HIV itself. In Botswana, 17% of the health workers died from diseases

related to AIDS from 1999 to 2005. The "Treat, Train, Retrain" global effort aims to prevent HIV among health workers and to treat those who are infected, to expand the workforce by training new people and by making more efficient use of the current pool of human resources for health, and to retain skilled staff. Possibly the most challenging imperative to expand the health workforce is the need for "task shifting", the process of delegation in which tasks are moved, where appropriate, from more to less specialized health workers. Reorganizing the force in this way allows more efficient use of available human resources and quickly expands the overall human resource pool. Although such programs are in their early days, there is evidence of success. In South Africa, care models that shift many medical tasks to nurses were found to be feasible, acceptable to patients, and potentially more affordable. After 6 months of follow-up, outcomes such as virologic suppression, adherence, and retention of patients at sites with doctors were similar to those at sites without doctors where there was adequate supervision. The process of delegation can further extended from health professionals to community members. Adopting new models for the delivery of health services requires political and financial commitment. Governments, as well as international and bilateral agencies, will need to recognize and allow systems that train and deploy nonphysicians, including community-level workers and patients living with HIV in health care delivery. Although research is needed in these areas, sufficient data are already available to support a prompt scale-up of HIV prevention, care, and treatment through task shifting to save as many lives as quickly as possible. **Editors' note: Although the term "task shifting" is new, the experience of task substitution has been documented since the 1970s in a variety of settings, often as a measure to enhance quality and reduce cost rather than as an emerging response to scarcity. Task shifting works best when standardized protocols, appropriate training, ongoing supervisory support, and a meaningful career pathway support it.**

7. Basic science

Bernstein A. AIDS and the next 25 years. *Science*. 2008; 320(5877):717.

Since HIV was discovered as the cause of AIDS a quarter century ago, over 60 million people have been infected with the virus and over 25 million people have died. These numbers make the result of two "proof of concept" vaccine efficacy trials—the STEP and Phambili trials—extremely disappointing. These results reflect our still-limited knowledge of HIV, its interactions with the human immune system, and the formidable, unprecedented challenges that it poses. But evidence of immunological protection in certain experimental models of HIV in nonhuman primates, and the intriguing observation that a small proportion of HIV-infected individuals ("elite controllers") can completely suppress the virus for years, suggest that a vaccine may be achievable. More, not less, basic and early-stage clinical research is needed. We need to understand the role of both the innate and adaptive immune responses during HIV infection. We need to make it much more attractive for young researchers, including those from other fields, to enter the HIV vaccine field. And the continued engagement of industry is essential if we are ever to have a vaccine. We know from experience with other pathogens that a vaccine is the best way to stop a virus. The only end for a journey that began 25 years ago should be the development of a safe and effective HIV vaccine. **Editors' Notes: Disappointment can lead to sober reflection and taking stock of what should remain a firm foundation and what can and should be challenged and changed. HIV has a high degree of sequence diversity and is a phenomenal foe,**

striking the very cells needed for an effective immune response. The stakes are high- this is not the time to walk away.

Walker BD, Burton DR. Toward an AIDS vaccine. *Science*. 2008; 320(5877):760-4.

A quarter century of scientific discovery has been applied to developing an AIDS vaccine, yet this goal remains elusive. Specific characteristics of the virus, including the extreme genetic variability in circulating viral isolates worldwide, biological properties of HIV that impede immune attack, and a high mutation rate that allows for rapid escape from adaptive immune responses, render this a huge challenge. However, evidence of protection against AIDS viruses in animal models and control of HIV in humans under certain circumstances, together with scientific advances in understanding disease pathogenesis, provide a strong rationale and objective paths to continue the pursuit of an effective AIDS vaccine to stem the global epidemic. **Editors' Notes: This review explains how the vaccines that work do so, before addressing the unique challenges for the development of an HIV vaccine. These include failure thus far to generate an immunogen to elicit effective neutralising antibodies and to identify the nature of T cell responses that could best contribute to vaccine protection against HIV. Nine critical issues and recommendations for immediate attention are laid out along with a call to pursue an HIV vaccine with greater passion than ever.**

Rossi JJ, June CH, Kohn DB. Genetic therapies against HIV. *Nat Biotechnol*. 2007; 25(12):1444-54

Highly active antiretroviral therapy prolongs the life of HIV-infected individuals, but it requires lifelong treatment and results in cumulative toxicities and viral-escape mutants. Gene therapy offers the promise of preventing progressive HIV infection by sustained interference with viral replication in the absence of chronic chemotherapy. Gene-targeting strategies are being developed with RNA-based agents, such as ribozymes, antisense, RNA aptamers and small interfering RNA, and protein-based agents, such as the mutant HIV Rev protein M10, fusion inhibitors and zinc-finger nucleases. Recent advances in T-cell-based strategies include gene-modified HIV-resistant T cells, lentiviral gene delivery, CD8(+) T cells, T bodies and engineered T-cell receptors. HIV-resistant hematopoietic stem cells have the potential to protect all cell types susceptible to HIV infection. The emergence of viral resistance can be addressed by therapies that use combinations of genetic agents and that inhibit both viral and host targets. Many of these strategies are being tested in ongoing and planned clinical trials. **Editors' note: The plot thickens! Gene therapy could be a stand-alone approach or an adjuvant to drug regimens. However, most people living with HIV today are in settings with insufficient infrastructure to support such technology and viral escape will confound even gene therapy approaches. Several clinical trials testing gene transfer strategies are underway, but don't hold your breath- this will take some time.**

8. Injecting drug use

Sylla L, Bruce RD, Kamarulzaman A, Altice FL. Integration and co-location of HIV/AIDS, tuberculosis and drug treatment services. *Int J Drug Policy* 2007; 18:306-12.

Injection drug use plays a critical role in the HIV epidemic in several countries throughout the world. In these countries, injection drug users are at significant risk for both HIV and tuberculosis, and active injection drug use negatively impacts treatment access, adherence,

and retention. Comprehensive strategies are therefore needed to effectively deliver preventive, diagnostic, and curative services to these complex patient populations. Sylla and colleagues propose that developing co-located integrated care delivery systems should become the focus of national programmes as they continue to scale-up access to antiretroviral medications for drug users. Existing data suggest that such a programme will expand services for each of these diseases; increase detection of tuberculosis and HIV; improve medication adherence; increase entry into substance use treatment; decrease the likelihood of adverse drug events; and improve the effectiveness of prevention interventions. Key aspects of integration programmes include: co-location of services convenient to the patient; provision of effective substance use treatment, including pharmacotherapies; cross-training of generalist and specialist care providers; and provision of enhanced monitoring of drug-drug interactions and adverse side effects. Central to implementing this agenda will be fostering the political will to fund infrastructure and service delivery, expanding street-level outreach to injection drug users, and training community health workers capable of cost effectively delivering these services. **Editors' note: The case for co-location of HIV, TB, and drug treatment services is strong. The "two diseases-one life" nomenclature for TB/HIV puts the focus on the patient, adding drug treatment services and reproductive health services recognises the need for integrated care for this complex and vulnerable patient population.**

9. Country responses

Russell TV, Do AN, Setik E, Sullivan PS, Rayle VD, Fridlund CA, Quan VM, Voetsch AC, Fleming PL. Sexual Risk Behaviors for HIV/AIDS in Chuuk State, Micronesia: The Case for HIV Prevention in Vulnerable Remote Populations. *PLoS ONE*. 2007; 2(12):e1283.

After the first two cases of locally-acquired HIV infection were recognized in Chuuk State, Federated States of Micronesia, a public health response was initiated. The purpose of the response was to assess the need for HIV education and prevention services, to develop recommendations for controlling further spread of HIV in Chuuk, and to initiate some of the prevention measures. A public health team conducted a survey and rapid HIV testing among a sample of residents on the outer islands in Chuuk. Local public health officials conducted contact tracing and testing of sex partners of the two locally-acquired cases of HIV infection. A total of 333 persons completed the survey. The majority knew that HIV is transmitted through unprotected sexual contact (81%), injection drug use (61%), or blood transfusion (64%). Sexual activity in the past 12 months was reported among 159 participants, including 90 females and 69 males. Compared to women, men were more likely to have had multiple sex partners, to have been drunk during sex, but less likely to have used a condom in the past 12 months. The two men with locally acquired HIV infection had unprotected anal sex with a third Chuukese man who likely contracted HIV while outside of Chuuk. All 370 persons who received voluntary, confidential HIV counselling and testing had HIV negative test results. Despite the low HIV seroprevalence, risky sexual behaviours in this small isolated population raise concerns about the potential for rapid spread of HIV. The lack of knowledge about risks, along with stigmatizing attitudes towards persons infected with HIV and high risk sexual behaviours indicate the need for resources to be directed toward HIV prevention in Chuuk and on other Pacific Islands. **Editors' note: With only 1500 residents living on this small group of islands, confidentiality would not have been maintained if classical "contact tracing and testing of sex partners", as implied by the abstract, had occurred. The innovation was for local village officials to convene a public**

meeting on each of the four islands to explain general health outreach activities, including the offer of HIV testing and counselling. When known contacts of either of the two index cases came forward for HIV testing, health department staff notified them of their potential exposure and provided expanded counselling on HIV risk reduction, without loss of confidentiality. Geographic isolation does not protect people from HIV and the constraints to respecting confidentiality in small populations need to be overcome creatively, as was done here.

10. Prevention programme design

Ickovics JR. « Bundling » HIV prevention: Integrating services to promote synergistic gain. *Prev Med* 2007; 46(3):222-5.

Bundling is defined as the aggregation of services to increase effectiveness (i.e., creating synergy of effort). Ickovics and colleagues aimed to review the utilization and potential benefits of bundling in its application to HIV prevention. A review of the literature was conducted to provide a broad perspective on the concept of bundling and specific examples of bundling in HIV prevention. Benefits, challenges, and directions were considered. To be effective, bundling must offer strategic advantage: greater value, less cost. It provides an opportunity to target multiple risk behaviours simultaneously for synergistic gain. Technological advances including rapid HIV tests permit non-invasive sampling in clinical and non-clinical settings. Bundling of HIV prevention provides an opportunity to reach high-risk persons who are asymptomatic and/or may not otherwise seek care by eliminating barriers to prevention. In conclusion, programmes that work must be implemented and innovative approaches considered to stem the AIDS epidemic; bundling provides one such opportunity to create an efficient paradigm targeting multiple risk behaviours simultaneously. **Editors' note: Bundling goods or services in business is done to increase profitability with customers benefiting from integrated value-added services, one-stop shopping, and lower prices. In HIV prevention, what gets bundled together, how and how much are important to programme effectiveness-it is high time to create synergy and secondary gain through thoughtful bundling.**

11. Treatment and care

Husbands W, Browne G, Caswell J, Buck K, Braybrook D, Roberts J, Gafni A, Taylor A. Case management community care for people living with HIV/AIDS (PLHAs). *AIDS Care* 2007; 19:1065-72.

A case management approach to support services was developed in a Toronto-based AIDS service organization in Canada to support people living with HIV whose needs could not be addressed through usual self-directed access to services. It was therefore important to determine which persons would benefit most from case management. New clients and those who had been receiving support services from an AIDS service organization were randomized to receive either self-directed use of support services or self-directed care plus strengths-based case management for a six-month period. Those who benefited most from case management were very depressed at baseline. Strengths-based case management compared to usual self-directed care markedly improved the physical, social, and mental health function of very depressed persons living with HIV, and reduced their risk behaviours. In addition, the case management participants' use of community services was associated with an economically important, though not statistically significant, \$3,300 per person per annum lower expenditure for the use of all direct health and social services. Although more

research is warranted, this research demonstrates that AIDS service organizations and funders ought to seriously consider implementing a case management approach to practical assistance for persons living with HIV with depression. **Editors' note: Placing very depressed patients with a case manager who can assist them in becoming functional was found to be good value for money invested and improved quality of life. The lower expenditure on all services used by people living with HIV who received case management more than offset the cost of case managers, under a system of national health care insurance.**

12. Paediatric treatment and care

Tejiokem MC, Gouandjika I, Béniguel L, Zanga MC, Tene G, Gody JC, Njamkepo E, Kfutwah A, Penda I, Bilong C, Rousset D, Pouillot R, Tangy F, Baril L. HIV-Infected Children Living in Central Africa Have Low Persistence of Antibodies to Vaccines Used in the Expanded Program on Immunization. *PLoS ONE*. 2007; 2(12):e1260.

The Expanded Program on Immunization is the most cost-effective measure to control vaccine-preventable diseases. Currently, the Expanded Program on Immunization schedule is similar for HIV-infected children; the introduction of antiretroviral therapy should considerably prolong their life expectancy. To evaluate the persistence of antibodies to the Expanded Program on Immunization vaccines in HIV-infected and HIV-exposed uninfected children who previously received these vaccines in routine clinical practice, Tejiokem and colleagues conducted a cross-sectional study of children, aged 18 to 36 months, born to HIV-infected mothers and living in Central Africa. The authors tested blood samples for antibodies to the combined diphtheria, tetanus, and whole-cell pertussis (DTwP), the measles and the oral polio (OPV) vaccines. They enrolled 51 HIV-infected children of whom 33 were receiving antiretroviral therapy, and 78 HIV-uninfected children born to HIV-infected women. A lower proportion of HIV-infected children than uninfected children had antibodies to the tested antigens with the exception of the OPV types 1 and 2. This difference was substantial for the measles vaccine (20% of the HIV-infected children and 56% of the HIV-exposed uninfected children, p<0.0001). There was a high risk of low antibody levels for all Expanded Program on Immunization vaccines, except OPV types 1 and 2, in HIV-infected children with severe immunodeficiency (CD4(+) T cells <25%). Children were examined at a time when their antibody concentrations to Expanded Program on Immunization vaccines would have still not undergone significant decay. However, the authors showed that the antibody concentrations were lowered in HIV-infected children. Moreover, antibody concentration after a single dose of the measles vaccine was substantially lower than expected, particularly low in HIV-infected children with low CD4(+) T cell counts. This study supports the need for a second dose of the measles vaccine and for a booster dose of the DTwP and OPV vaccines to maintain the antibody concentrations in HIV-infected and HIV-exposed uninfected children. **Editors' note: Although more research is needed to better understand altered immune responses in uninfected infants born to HIV-positive women, it is clear from this study that there is an urgent need to study the effects of early initiation of antiretroviral therapy on responses to vaccines in children with HIV infection. In the meantime, booster doses would seem a pragmatic approach.**

Wachholz NI, Ferreira J. Adherence to antiretroviral therapy in children: a study of prevalence and associated factors. *Cad Saude Publica*. 2007; 23 Suppl 3:S424-34.

The survival of children with HIV has increased considerably with the use of more effective antiretrovirals, but the benefits of this therapy are limited by the difficulty of adherence to the treatment. This cross-sectional study aimed to estimate the prevalence of non-adherence to antiretrovirals among children residents in Porto Alegre, Rio Grande do Sul State, Brazil, and identifying associated factors. There were 194 child caregivers interviewed. The technique utilized to evaluate adherence allowed the detection of lack of understanding of the prescribed antiretroviral regimens, as well as conscious loss of doses. Non-adherence was defined when the child had taken less than 80% of the prescribed medication during the 24 h period prior to the interview. A general prevalence of non-adherence was 49.5%, which was higher than that estimated. The non-institutional caregivers had a prevalence rate of 55.7%, while the institutional caregivers had 22.2%. In multivariate analysis, the education of the caregiver was found to have a borderline association with the outcome. Institutionalized children and those taken care of by people with a higher educational level appeared to have more protection against non-adherence to antiretroviral therapy. **Editors' note: For a country that guarantees free access to antiretroviral drugs, this high non-adherence rate is surprising. Non-adherence to antiretroviral treatment in children is clearly dependent on caretaker knowledge, attitudes, and behaviour. These are in part influenced by the type (relative or not) and quality of relationship between the caregiver and the child, and educational level of the caregiver. A stronger emphasis on monitoring caregivers is needed to protect children.**

Orem J, Mbidde EK, Lambert B, de Sanjose S, Weiderpass E. Burkitt's lymphoma in Africa, a review of the epidemiology and etiology. *Afr Health Sci*. 2007; 7(3):166-75.

Burkitt's lymphoma was first described in Eastern Africa, initially thought to be a sarcoma of the jaw. Shortly it became well known that this was a distinct form of Non Hodgkin's lymphoma. The disease has given insight in all aspects of cancer research and care. Its peculiar epidemiology has led to the discovery of Epstein Barr virus and its importance in the cause of several viral illnesses and malignancies. The highest incidence and mortality rates of Burkitt's lymphoma are seen in Eastern Africa. Burkitt's lymphoma affects mainly children, and boys are more susceptible than girls. Evidence for a causal relationship between Epstein Barr virus and Burkitt's lymphoma in the endemic form is fairly strong. Frequency of association between Epstein Barr virus and Burkitt's lymphoma varies between different patient groups and different parts of the world. Epstein Barr virus may play a role in the pathogenesis of Burkitt's lymphoma by deregulation of the oncogene c-MYC by chromosomal translocation. Although several studies suggest an association between malaria and Burkitt's lymphoma, there has never been a conclusive population study in support of a direct role of malaria in causation of Burkitt's lymphoma. The emergence of HIV and a distinct subtype of Burkitt's lymphoma in HIV-infected have brought a new dimension to the disease particularly in areas where both HIV and Burkitt's lymphoma are endemic. Burkitt's lymphoma has been reported as a common neoplasm in HIV-infected patients, but not in other forms of immunodepression, and the occurrence of Burkitt's lymphoma seems to be higher amongst HIV-positive adults, while the evidence of an association amongst children is still disputed. The role of other possible risk factors such as low socio-economical status, exposure to a plant species common in Africa called Euphorbiaceae, exposure to pesticides and to other infections such as schistosomiasis and arbovirus (an RNA virus transmitted by insect vectors) remain to be elucidated. **Editors' note: Burkitt's lymphoma, which affects mainly children in Eastern Africa, is on the rise suggesting a possible association with HIV**

infection. In adults, increasing incidence has been seen in both Kenya and Uganda, which is not surprising given HIV prevalence and the known association between Epstein Barr virus infection and Burkitt's lymphoma.

13. Structural determinants and vulnerability

Zungu-Dirwayi N, Shisana O, Louw J, Dana P. Social determinants for HIV prevalence among South African educators. *AIDS Care*. 2007; 19(10):1296-303.

HIV prevalence among women in South Africa continues to be high despite the availability of a comprehensive plan for the control of HIV and a plethora of prevention programmes. Any explanation for the ongoing high HIV prevalence continues to be elusive. The objective of this study was to understand the relationship between HIV, gender, race, and socioeconomic status among South African public sector educators in order to inform prevention programmes. A cross-sectional survey involving a probability sample of 1,766 schools out of 26,713 in the Department of Education Register of School Needs was selected. A sample of 24,200 respondents out of 356,749 public sector educators participated in the study. Nurses registered with the South African Nursing Council were recruited, trained to conduct interviews and to collect specimens for HIV testing. The study found an association between HIV, gender, race, and socioeconomic status among educators. African educators showed a higher HIV prevalence than other race groups. Among females, the highest HIV prevalence was among educators aged 25-35 years and in males aged 36-49 years. Further, educators with a high income and educational qualifications had a lower HIV prevalence compared to educators with low income and low educational qualifications, regardless of sex. Migration and marital factors were also found to play a role in HIV infection. The results suggest that HIV prevention needs to take into account critical issues around empowerment of vulnerable groups such as women and certain race groups to be able to implement safe sexual practices and therefore reduce HIV infections. **Editors' note: Nearly 13% of all educators were HIV-positive in this study, a tremendous toll for any educational system. HIV prevalence in women who began teaching being married (14.7%) or engaged (11.4%) was lower than that among those who began their career being single (25.4%). Prevention programmes for young, single, female educators who are mobile are urgently needed. Educators of both sexes who were placed away from their families on completion of their studies had a significantly higher HIV prevalence. School boards need to consider the advantages of keeping teachers' families with them to preserve mid-to-long term teaching capacity.**

Oyefara JL. Food insecurity, HIV/AIDS pandemic and sexual behaviour of female commercial sex workers in Lagos metropolis, Nigeria. *SAHARA J*. 2007; 4(2):626-35.

This study examined the role of hunger and food insecurity in the sexual behaviour of female sex workers in Lagos metropolis, Nigeria within the context of HIV. In addition, the study investigated the prevalence of sexually transmitted infections and induced abortion among the respondents. Cross-sectional survey and in-depth interview research methods were adopted to generate both quantitative and qualitative data from the respondents. The study showed that 35.0% of the respondents joined the sex industry because of poverty and lack of other means of getting daily food. While all the respondents had knowledge about the existence of HIV and AIDS, 82.0% of them identified sexual intercourse as a major route of HIV transmission. There was a significant relationship between poverty, food insecurity, and consistent use of condoms by female sex workers at $P < 0.01$. Specifically, only 24.7% of the

respondents used condoms regularly in every sexual act. Consequently, 51.6% had previous cases of sexually transmitted infections. The most prevalent sexually transmitted infection among the respondents was gonorrhoea, with 76.4% prevalence among ever infected female sex workers. This was followed by syphilis with a prevalence of 21.1%. In addition, 59.1% of the sample had become pregnant while on the job and 93.1% of these pregnancies were aborted through induced abortion. In conclusion, hunger and malnutrition were the factors that pushed young women into prostitution in Nigeria and these same factors hindered them from practicing safe sex within the sex industry. Thus, it is recommended that the Nigerian government should develop programmes that will reduce hunger and food insecurity, in order to reduce rapid transmission of HIV infection in the country. **Editors' note: The links between hunger, food insecurity, and vulnerability to HIV described by this article are brought into sharp relief by the current global food crisis. Improving local food production to meet basic food needs not only helps reduce poverty levels; it pulls the rug out from under food insecurity as a driver of the HIV epidemic.**

14. Stigma

Lau JT, Choi KC, Tsui HY, Su X. Associations between stigmatization toward HIV-related vulnerable groups and similar attitudes toward people living with HIV/AIDS: Branches of the same tree? *AIDS Care*. 2007; 19(10):1230-40.

This study tested the hypothesis that stigmatization toward people living with HIV (PLHIV) was associated with stigmatization toward different vulnerable groups, including men who have sex with men, injecting drug users, female sex workers, and their clients. A number of scales and indicators were constructed for the purpose: the four Overall Stigmatization Scale for a Vulnerable Group (OSSVG) and the five Dimensional Stigmatization Scale (DSS) each measuring different dimensions of stigmatization toward the four vulnerable groups, together with four indicators measuring stigmatization toward PLHIV. A random sample of 2,008 Hong Kong Chinese adults aged 18-50 years in the general population were interviewed by telephone. Of these respondents, 22.8-76.8% perceived that female sex workers, clients of female sex workers, men who have sex with men and injecting drug users were pathological and 42-82.2% perceived them as immoral; 74.7% believed that PLHIV are promiscuous. Furthermore, the four OSSVG and the five DSS scales were inter-correlated with one another (Spearman coefficient = 0.11-0.67) and most of them were significantly associated with the four PLHIV stigmatization indicators (Odds Ratio = 1.25-4.27). Other factors were associated with the OSSVG and DSS scores (e.g. age, marital status, religion affiliation, education level, income and perceived severity of the HIV problem in Hong Kong). Campaigns for removing stigmatization toward these vulnerable groups are required in order to reduce stigmatization toward PLHIV. Stigmatization toward female sex workers and their clients might have been over-looked. The removal of the public's blame on these groups for spreading HIV may be useful. The impact of HIV prevalence of a vulnerable group onto the associations between stigmatization toward that particular group and PLWHA warrants investigation. **Editors' note: Layered stigmatisation or discrimination, attributed both to features of HIV and to non-HIV components such as how one contracted HIV infection, has not been well studied. Stigma is discrediting, reduces status in society, and is disempowering. This study did not examine discriminatory behaviours, but rather discriminatory attitudes or stigmatization, which can nonetheless be very harmful in Hong Kong society, as elsewhere. Effective community mobilisation and social change communication is required to address layered stigmatization.**

That was *HIV This Week*, signing off.

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