

HIV This Week: what scientific journals said

Welcome to the 69th issue of *HIV This Week*! In this issue, we cover *men who have sex with men* (time to act: an innovative study in Malawi, Namibia, and Botswana links HIV and human rights abuses; does anal human papilloma virus infection increase risk for HIV acquisition?; sex drugs and HIV risk: effects beyond drug-induced disinhibition?), *biomedical prevention tools* (efficacious drug delivery through vaginal rings; the 'female condom' and anal sex), *behavioural change: mobilising men* (Nigerian men respond to a culturally-tailored intervention; South African men respond in different ways to gender-based violence and alcohol reduction interventions), *epidemiology* (5 years of sustained high HIV incidence in a rural KwaZulu Natal community cause for concern; how data from Uganda's antenatal surveillance and national population-based survey compare; was there a second HIV incidence peak in Thailand due to the Asian financial crisis?), *tuberculosis* (survival improves with earlier HIV treatment and care for co-infected Thai TB patients), *health care delivery* (male circumcision training: practice makes perfect; a paediatric AIDS corps treating kids in Botswana, Lesotho, Swaziland, Malawi, and Burkina Faso; lessons learned about improving sexual assault services in rural South Africa), *novel treatment approaches: gene therapy* (glimmers of light from a Phase II anti-HIV ribozyme trial), *workplace responses* (a toast to a pioneer private sector HIV workplace programme in Africa), *HIV transmission on antiretroviral treatment* (an estimated risk of 1 in 7900 heterosexual acts?; community viral load in Vancouver's downtown eastside mirrors HIV incidence in individual injecting drug users), *communications* (22,894 storylines for films reveal how young Africans perceive HIV), *blood donor deferral* (science sheds light on blood donation deferral periods for men who have sex with men), and *human rights* (how and why structural-rights interventions should underpin combination prevention and treatment in Zimbabwe and everywhere else).

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Cate Hankins

Chief Scientific Adviser

Nicolai Lohse

Research Officer

Tania Lemay

Research Consultant

1. *Men who have sex with men*

Baral S, Trapence G, Motimedi F, Umar E, Iiping S, Dausab F, Beyrer C. HIV prevalence, risks for HIV infection, and human rights among men who have sex with men (MSM) in Malawi, Namibia, and Botswana. *PLoS ONE*. 2009;4(3):e4997.

In the generalized epidemics of HIV in southern sub-Saharan Africa, men who have sex with men have been largely excluded from HIV surveillance and research. Epidemiologic data for men who have sex with men in southern Africa are among the sparsest globally, and HIV risk among these men has yet to be characterized in the majority of countries. A cross-sectional anonymous probe of 537 men recruited with non-probability sampling among men who reported ever having had sex with another man was conducted in Malawi, Namibia, and Botswana using a structured survey instrument and HIV screening with the OraQuick® rapid test kit. The HIV prevalence among those between the ages of 18 and 23 was 8.3% (20/241); 20.0% (42/210) among those 24-29; and 35.7% (30/84) among those older than 30 for an overall prevalence of 17.4% (95% CI 14.4-20.8). In multivariate logistic regressions, being older than 25 (aOR 4.0, 95% CI 2.0-8.0), and not always wearing condoms during sex (aOR 2.6, 95% CI 1.3-4.9) were significantly associated with being HIV-positive. Sexual concurrency was common with 16.6% having ongoing concurrent stable relationships with a man and a woman and 53.7% had both male and female sexual partners in proceeding 6 months. Unprotected anal intercourse was common and the use of petroleum-based lubricants was also common when using condoms. Human rights abuses, including blackmail and denial of housing and health care was prevalent with 42.1% (222/527) reporting at least one human rights abuse. Men who have sex with men are at higher risk of HIV exposure for HIV infection and human rights abuses in Malawi, Namibia, and Botswana. Concurrency of sexual partnerships with partners of both genders may play important roles in HIV spread in these populations. Further epidemiologic and evaluative research is needed to assess the contribution of men who have sex with men to southern Africa's HIV epidemics and how best to mitigate this. These countries should initiate and adequately fund evidence-based and targeted HIV prevention programs for men who have sex with men. **Editors' note: This simple epidemiology and human rights study, the first to link individual level rights abrogation to HIV biological outcomes in the African context, was implemented through collaboration with local community groups and can be replicated in similar settings. The overall findings of a high risk of exposure to both HIV and human rights abuses, in these three high HIV prevalence countries that criminalize same sex behaviour among consenting adults, are striking. Effective HIV prevention programming for men who have sex with men, particularly younger men, in Botswana, Malawi, and Namibia requires urgent governmental attention with dedicated funding and creative innovations, including use of the internet to reach this hidden population, training of health care providers, and strategies to address and minimise human rights abuses.**

Chin-Hong PV, Husnik M, Cranston RD, Colfax G, Buchbinder S, Da Costa M, Darragh T, Jones D, Judson F, Koblin B, Mayer KH, Palefsky JM. Anal human papillomavirus infection is associated with HIV acquisition in men who have sex with men. *AIDS*. 2009 Apr 22. [Epub ahead of print]

Human papillomavirus is a common sexually transmitted agent that causes anogenital cancer and pre-cancer lesions that have an inflammatory infiltrate, may be friable, and bleed. Chin-Hong and colleagues aimed to determine the association between anal HPV infection and HIV acquisition using a prospective cohort study design. They recruited 1409 HIV-negative men

who have sex with men from a community-based setting in Boston, Denver, New York, and San Francisco. The authors used Cox proportional hazards regression modeling and assessed the independent association of HPV infection with the rate of acquisition of HIV infection. Of 1409 participants contributing 4375 person-years of follow-up, 51 HIV-seroconverted. The median number of HPV types in HPV-infected HIV-seroconverters was 2 (interquartile range 1-3) at the time of HIV seroconversion. After adjustment for sexual activity, substance use, occurrence of other sexually transmitted infections, and demographic variables, there was evidence (P = 0.002) for the effect of infection with at least two HPV types (hazard ratio 3.5, 95% confidence interval 1.2-10.6) in HIV seroconversion. The authors conclude that anal HPV infection is independently associated with HIV acquisition. Studies that incorporate high-resolution anoscopy to more accurately identify HPV-associated disease are needed to determine the relationship between HPV-associated disease and HIV seroconversion. **Editors' note: HPV disease has long been considered to be opportunistic, taking advantage of HIV-induced immunosuppression but not increasing the risk of HIV acquisition. If, as this first study to do so suggests, anal HPV infection is independently associated with HIV acquisition, immunizing HPV-unexposed people to prevent invasive cancer and anogenital warts may have the potential to reduce the risk of HIV acquisition through anal sex.**

Ostrow DG, Plankey MW, Cox C, Li X, Shoptaw S, Jacobson LP, Stall RC. Specific Sex Drug Combinations Contribute to the Majority of Recent HIV Seroconversions Among MSM in the MACS. *J Acquir Immune Defic Syndr*. 2009 Apr 21. [Epub ahead of print]

New HIV infections are being observed among men who have sex with men (MSM). Understanding the fusion of risky sexual behaviours, stimulant drug use, and erectile dysfunction drug use with HIV seroconversion may provide direction for focused intervention. During the follow-up period (1998-2008), Ostrow and colleagues identified 57 HIV seroconverters among 1667 initially HIV-seronegative men. Time to seroconversion was modelled using Cox proportional hazards regression analysis for 7 combinations of sex drugs (inhaled nitrites or "poppers", stimulants, and erectile dysfunction drugs) used at the current or previous semi-annual visit, adjusting for other risk factors including sexual behaviour, alcohol and other drugs used, and depression. Model-based adjusted attributable risks were then calculated. The risk of seroconversion increased linearly with the number of unprotected receptive anal sex partners, with hazard ratios ranging from 1.73 [95% confidence interval (CI): 0.75 to 4.01] for 1 partner, to 4.23 (95% CI: 1.76 to 10.17) for 2-4 partners, and to 14.21 (95% CI: 6.27 to 32.20) for 5+ partners, independent of other risk factors. After adjustment, risks for seroconversion increased from 2.99 (95% CI: 1.02 to 8.76) for men who reported using stimulants only (1 drug) to 8.45 (95% CI: 2.67 to 26.71) for men who reported using all 3 sex drugs. The use of any of the 7 possible sex drug combinations accounted for 63% of the 9-year HIV seroincidence in the Multicenter AIDS Cohort Study. When contributions of increased unprotected receptive anal sex partners and combination drug use were analyzed together, the total attributable risk for HIV seroconversion was 74%, with 41% attributable to unprotected receptive anal sex partners alone and a residual of 33% due to other direct or indirect effects of sex drug use. Use of poppers, stimulants, and erectile dysfunction drugs increased risk for HIV seroconversion significantly in this cohort. These data reinforce the importance of implementing interventions that target drug reduction as part of comprehensive and efficacious HIV prevention strategies. **Editors' note: Whether or not and how vasoactive sex drug use**

could increase the likelihood of HIV infection through unprotected sex, over and above the disinhibiting effects of drug use, is unclear. Nonetheless, the magnitude of the risk posed by the use of stimulant, poppers, and erectile dysfunction drugs is clear - among men who used all three drugs the relative hazard for HIV seroconversion was 8 times that of men who reported no use of these sex drugs. With noninjection substance use seemingly on the increase among men who have sex with men, particularly the use of erectile dysfunction drugs as men age, attention addressed to the linked epidemics of substance use and high-risk sex should inform tailored harm reduction and safer sex strategies.

2. Biomedical prevention tools

Saxena BB, Han YA, Fu D, Rathnam P, Singh M, Laurence J, Lerner S. Sustained release of microbicides by newly engineered vaginal rings. *AIDS*. 2009 Apr 17. [Epub ahead of print]

An effective vaginal microbicide against sexual HIV transmission remains elusive, with requirements for adherence to appropriate application of effective, nontoxic products being a major deterrent. Saxena and colleagues explored methods to enable sustained release of combinations of antiretroviral microbicides, utilizing intravaginal rings composed of biosoluble Acacia gum or non-biodegradable hydrogel of 2-hydroxyethyl methacrylate and sodium methacrylate, materials approved for use by the United States Food and Drug Administration. The reverse transcriptase inhibitors TMC120, PMPA, 3'-azido-3'-deoxythymidine, and a newly characterized anti-HIV agent, Boc-lysinated betulonic acid, were incorporated into vaginal rings with different combinations. Daily and cumulative release rates of these inhibitors in ring eluates were determined by high-performance liquid chromatography, gas chromatography, or immunoassay. Anti-HIV effects were measured by assessment of p24 Gag antigen in T-cell cultures exposed to HIV-1 isolates. Drug release rates were sustained at concentrations higher than the minimum effective dose for HIV inhibition. The release was maintained for no less than 15 and 28 days from the Acacia gum and 2-hydroxyethyl methacrylate and sodium methacrylate rings, respectively. Boc-lysinated betulonic acid showed more than 90% inhibition of HIV-1 infection in H9 cells, with little toxicity to normal cells. The intravaginal rings described here are capable of efficacious drug delivery. Incorporation of several antiretroviral agents, including betulinol derivatives, which act at multiple levels of the HIV life cycle, may provide a synergistic effect to achieve higher efficacy on the inhibition of HIV infection. **Editors' note: Although many participants in microbicide gel trials report the unexpected benefit of improved sexual satisfaction with gel use, work is proceeding with alternate microbicide delivery systems that have other potential advantages. Those include sustained delivery through a ring that could be put into position monthly, for example. Not having to insert a microbicide before each sex act would likely appeal to many women, particularly if the vaginal ring releases locally active, effective, and safe antiretroviral drugs for prevention.**

Kelvin EA, Smith RA, Mantell JE, Stein ZA. Adding the Female Condom to the Public Health Agenda on Prevention of HIV and Other Sexually Transmitted Infections Among Men and Women During Anal Intercourse. *Am J Public Health*. 2009 Apr 16. [Epub ahead of print]

Legal barriers to conducting public health research on methods of protection for anal intercourse were lifted in the United States in 2003 when the US Supreme Court invalidated all state antisodomy laws. Although research funding has been available for the development of rectal microbicides, the female condom, which has already been approved for vaginal use,

has not been evaluated for anal use. Although there is no evidence that the female condom is safe for anal intercourse, it has already been taken up for off-label use by some men who have sex with men. This demonstrates the urgent need for more protection options for anal intercourse and, more immediately, the need to evaluate the safety and efficacy of the female condom for anal intercourse. **Editors' note: Among men aged 25 to 44 years in the USA, 3.9% report having had anal sex with another man and 40% report having had anal sex with a woman. It is estimated that four times as many women in the USA practice anal sex than do men who have sex with men. Although the 'female condom' is recommended by some health providers and health promoters for anal sex, it has not been assessed for safety, ease of insertion (for example, should the inner ring be removed?), or efficacy. With the development and testing of rectal microbicides lagging behind vaginal products, quick studies to determine the optimal method for using the female condom during anal intercourse are needed now.**

3. Behavioural change: mobilising men

Exner TM, Mantell JE, Adeokun LA, Udoh IA, Ladipo OA, Delano GE, Faleye J, Akinpelu K. Mobilizing men as partners: the results of an intervention to increase dual protection among Nigerian men. *Health Educ Res.* 2009 Apr 9. [Epub ahead of print]

This quasi-experimental, proof-of-concept study evaluated the effects of an intervention designed to help Nigerian men decrease risk for HIV, sexually transmitted infections, and unintended pregnancy. The intervention was delivered in groups during two 5-hour workshops, with a monthly 2-hour check-in session. A comparison condition consisted of a group-based half-day didactic workshop. Based on recruitment area, 149 men were assigned to the intervention and 132 to the comparison. Men were evaluated at baseline and 3-month post-intervention. At follow-up, men assigned to the intervention were almost four times more likely than comparison men to report condom use at last intercourse (P < 0.001) and to report fewer unprotected vaginal sex occasions, greater self-efficacy for negotiation, a more egalitarian power dynamic in their primary relationship, more positive expectations for condom use, and greater intention for future consistent condom use (all P values < 0.05). Findings suggest that this intervention is both feasible and effective. **Editors' note: In addition to reducing HIV-related stigmatizing beliefs, this group-based cognitive-behavioural 'mobilising men as partners' intervention, tailored to the needs and culture of Nigerian men, resulted in significantly higher safer-sex self-efficacy and yet significantly less male-dominated power dynamics in primary relationships. Whether the results seen at 3 months would be sustained over time, whether there was community level influence supporting the positive changes (the intervention men were from different communities than the control men), and whether their female partners would corroborate the findings are all questions deserving further investigation.**

Kalichman SC, Simbayi LC, Cloete A, Clayford M, Arnolds W, Mxoli M, Smith G, Cherry C, Shefer T, Crawford M, Kalichman MO. Integrated Gender-Based Violence and HIV Risk Reduction Intervention for South African Men: Results of a Quasi-Experimental Field Trial. *Prev Sci.* 2009 Apr 8. [Epub ahead of print]

South Africa is in the midst of one of the world's most devastating HIV epidemics and there is a well-documented association between violence against women and HIV transmission. Interventions that target men and integrate HIV prevention with gender-based violence prevention may demonstrate synergistic effects. A quasi-experimental field intervention

trial was conducted with two communities randomly assigned to receive either: (a) a five session integrated intervention designed to simultaneously reduce gender-based violence and HIV risk behaviours (N = 242) or (b) a single 3-hour alcohol and HIV risk reduction session (N = 233). Men were followed for 1-, 3-, and 6-months post intervention with 90% retention. Results indicated that the gender-based violence/HIV intervention reduced negative attitudes toward women in the short term and reduced violence against women in the longer term. Men in the gender-based violence/HIV intervention also increased their talking with sex partners about condoms and were more likely to have been tested for HIV at the follow-ups. There were few differences between conditions on any HIV transmission risk reduction behavioural outcomes. Further research is needed to examine the potential synergistic effects of alcohol use, gender violence, and HIV prevention interventions. **Editors' note: Negative attitudes toward women in South Africa and societal acceptance of violence against women impede men from acting responsibly to reduce HIV risks for themselves and their partners. More than half of the men in this study reported a history of physically assaulting a sex partner and one in five had been detained for domestic violence. Although the study had an inherently weak study design (randomising two communities but examining individual level behaviour change), was conducted in one cultural group only (Xhosa), and 89% of the participants were unemployed and able to attend lengthy workshops, the findings are intriguing. The gender-based violence prevention group reported a number of positive changes in attitudes and behaviours toward women, but the alcohol prevention group appears to have offered greater potential for sexual risk reduction. A three-component programme of HIV sexual risk reduction, alcohol reduction, and gender violence prevention may achieve greater impact. However, until South Africa and other countries worldwide intervene effectively to penalise gender-based violence and create new social norms of respect and gender equality, counting on individual behaviour change alone is like swimming upstream against powerful currents.**

4. *Epidemiology*

Bärnighausen T, Tanser F, Newell ML. Lack of a Decline in HIV Incidence in a Rural Community with High HIV Prevalence in South Africa, 2003-2007. *AIDS Res Hum Retroviruses*. 2009 Mar 25. [Epub ahead of print]

To understand the dynamics of the HIV epidemic and to plan HIV treatment and prevention programs, it is critical to know how HIV incidence in a population evolves over time. Bärnighausen and colleagues used data from a large population-based longitudinal HIV surveillance in a rural community in South Africa to test whether HIV incidence in this population has changed in the period from 2003 through 2007. They observed 563 seroconversions in 8095 individuals over 16,256 person-years at risk, yielding an overall HIV incidence of 3.4 per 100 person-years (95% confidence interval 3.1-3.7). The authors included time-dependent period dummy variables (in half-yearly increments) in age-stratified Cox regressions in order to test for trends in HIV incidence. They first did regression analyses separately for women and men. In both regressions, the coefficients of all period dummy variables were individually insignificant (all $p \geq 0.338$) and jointly insignificant ($p = 0.764$ and $p = 0.111$, respectively). They then did regression analysis using the pooled data on women and men, controlling for sex and interactions between sex and age. Again, the coefficients of the eight period dummy variables were individually insignificant (all $p \geq 0.387$) and jointly insignificant ($p = 0.701$). They show for the first time that high levels of

HIV incidence have been maintained without any sign of decline over the past 5 years in both women and men in a rural South African community with high HIV prevalence. It is unlikely that the HIV epidemic in rural South Africa can be reversed without new or intensified efforts to prevent HIV infection. **Editors' note: Changes in HIV prevalence figures are difficult to interpret as they reflect both the incidence of new infections and mortality in people living with HIV. What we really need to know is the trend in HIV incidence as this reflects the effectiveness of prevention programming and predicts eventual treatment demand. The findings from this prospective, longitudinal study are highly disturbing: with a constant, unrelenting incidence of 3.4 per 100 person-years, 15 out of every 100 people who were HIV-negative at the start of the study in 2003 had seroconverted by its end 5 years later. The prevention programmes that have been operating clearly do not reach enough people with effective prevention messages, skills building, and support for changed sexual behaviour norms. Safe male circumcision services, positive prevention programmes, and community mobilisation to address the structural factors underlying risk in this rural KwaZulu-Natal community are additional approaches that deserve immediate attention.**

Musinguzi J, Kirungi W, Opio A, Montana L, Mishra V, Madraa E, Biryahwaho B, Mermin J, Bunnell R, Cross A, Hladik W, McFarland W, Stoneburner R. Comparison of HIV Prevalence Estimates From Sentinel Surveillance and a National Population-Based Survey in Uganda, 2004-2005. *J Acquir Immune Defic Syndr.* 2009 Mar 26. [Epub ahead of print]

HIV programs in generalized epidemics have traditionally relied on antenatal clinic sentinel surveillance data to guide prevention and to model epidemic trends. Antenatal clinic data, however, come from a subset of the population, and their representativeness of the population has been debated. Musinguzi et al compared data from a national population-based Uganda HIV Sero-Behavioral Survey with those from antenatal clinic sentinel surveillance. Using geographic information system, Uganda HIV Sero-Behavioral Survey clusters within a 30 km radius of the antenatal clinic sites were mapped. Estimates of HIV prevalence from antenatal clinic surveillance were compared with those from Uganda HIV Sero-Behavioral Survey. They found that the antenatal clinic-based HIV prevalence, 6.0% [confidence interval (CI) 5.5% to 6.5%], was similar to that from Uganda HIV Sero-Behavioral Survey, 5.9% (CI 5.4% to 6.4%). The antenatal clinic-based estimate correlated with that of Uganda HIV Sero-Behavioral Survey catchment area women who were pregnant and those who had given birth in the 2 years preceding the survey. Antenatal clinic data overestimated prevalence in the 15-year to 19-year age group, were similar to Uganda HIV Sero-Behavioral Survey for ages 20-29 years, and underestimated prevalence in older respondents. Antenatal clinic data underestimated HIV prevalence among women (6.0% vs. 7.4%; CI 6.6% to 8.2%) and urban women (7.6% vs. 12.7%) but was similar for rural women (5.3% vs. 4.9%). Antenatal clinic -based surveillance remains an important tool for monitoring HIV programs. Antenatal clinic and Uganda HIV Sero-Behavioral Survey data were similar overall and for 15-year to 29-year olds, women who were pregnant, and women who had a birth in the 2 years before the survey. Antenatal clinic estimates were lower in those ≥ 30 years and in urban areas. Periodic serosurveys to adjust antenatal clinic -based estimates are needed. **Editors' note: In a mature epidemic such as Uganda's, antenatal surveillance is likely to underestimate HIV prevalence in older women because older women can be at significant risk of acquiring HIV after the reproductive age and women with HIV who are of reproductive age tend to have lower fertility. Antenatal surveillance does generally reflect the**

general population prevalence among 15 to 29 year olds and in the age group 15 to 19 years it can be used as a general proxy measure of HIV incidence. Thus, antenatal clinic surveillance, supplemented by periodic population-based sero-behavioural surveys to provide an adjusted picture of national HIV epidemics, remains a valid surveillance tool.

Punyacharoensin N, Viwatwongkasem C. Trends in three decades of HIV/AIDS epidemic in Thailand by nonparametric backcalculation method. *AIDS*. 2009 Apr 17. [Epub ahead of print]

To reconstruct the past HIV incidence and prevalence in Thailand from 1980 to 2008 and predict the country's AIDS incidence from 2009 to 2011, nonparametric backcalculation was adopted utilizing 100 quarterly observed new AIDS counts excluding paediatric cases. The accuracy of data was enhanced through a series of data adjustments using the weight method to account for several surveillance reporting issues. The mixture of time-dependent distributions allowed the effects of age at seroconversion and antiretroviral therapy to be incorporated simultaneously. Sensitivity analyses were conducted to assess model variations that were subject to major uncertainties. Future AIDS incidence was projected for various predetermined HIV incidence patterns. HIV incidence in Thailand reached its peak in 1992 with approximately 115 000 cases. A steep decline thereafter discontinued in 1997 and was followed by another strike of 42 000 cases in 1999. The second surge, which happened concurrently with the major economic crisis, brought on 60 000 new infections. As of December 2008, more than 1 million individuals had been infected and around 430 000 adults were living with HIV corresponding to a prevalence rate of 1.2%. The incidence rate had become less than 0.1% since 2002. The backcalculated estimates were dominated by postulated median AIDS progression time and adjustments to surveillance data. The authors' analysis indicated that, thus far, the 1990s was the most severe era of HIV epidemic in Thailand with two HIV incidence peaks. A drop in new infections led to a decrease in recent AIDS incidence, and this tendency is likely to remain unchanged until 2011, if not further. **Editors' note: Backcalculation reconstructs a past pattern of HIV incidence based on AIDS surveillance data and a plausible incubation period from HIV infection to AIDS diagnosis. The relatively short incubation period of 7 years used in this work may have lowered the estimates of backcalculated total infections. Although it makes logical sense that the large cuts of one-third to one-half in government HIV prevention budgets during the financial crisis of 1998 to 2000 could have led to an intriguing second peak in HIV incidence in Thailand, further study is needed to confirm this.**

5. Tuberculosis

Varma JK, Nateniyom S, Akksilp S, Mankattitham W, Sirinak C, Sattayawuthipong W, Burapat C, Kittikraisak W, Monkongdee P, Cain KP, Wells CD, Tappero JW. HIV care and treatment factors associated with improved survival during TB treatment in Thailand: an observational study. *BMC Infect Dis*. 2009 Apr 13;9(1):42. [Epub ahead of print]

In Southeast Asia, HIV-infected patients frequently die during tuberculosis treatment. Many physicians are reluctant to treat HIV-infected tuberculosis patients with antiretroviral therapy and have questions about the added value of opportunistic infection prophylaxis to antiretroviral therapy, the optimum antiretroviral therapy regimen, and the benefit of initiating antiretroviral therapy early during tuberculosis treatment. Varma and colleagues conducted a multi-center observational study of HIV-infected patients newly diagnosed with tuberculosis in Thailand. Clinical data was collected from the beginning to the

end of tuberculosis treatment. They conducted multivariable proportional hazards analysis to identify factors associated with death. Of 667 HIV-infected tuberculosis patients enrolled, 450 (68%) were smear and/or culture positive. Death during tuberculosis treatment occurred in 112 (17%). In proportional hazards analysis, factors strongly associated with reduced risk of death were antiretroviral therapy use (Hazard Ratio [HR] 0.16; 95% confidence interval [CI] 0.07-0.36), fluconazole use (HR 0.34; CI 0.18-0.64), and cotrimoxazole use (HR 0.41; CI 0.20-0.83). Among 126 patients that initiated antiretroviral therapy after tuberculosis diagnosis, the risk of death increased the longer that antiretroviral therapy was delayed during tuberculosis treatment. Efavirenz- and nevirapine-containing antiretroviral therapy regimens were associated with similar rates of adverse events and death. Among HIV-infected patients living in Thailand, the single most important determinant of survival during TB treatment was the use of antiretroviral therapy. Controlled clinical trials are needed to confirm our findings that early antiretroviral therapy initiation improves survival and that the choice of non-nucleoside reverse transcriptase inhibitor does not. **Editors' note: The sequential arm (antiretroviral treatment given after 6 to 8 months of TB treatment) has already been shut down in one randomised controlled trial (SAPIT at CAPRISA, South Africa) due to a 55% lower mortality in the two integrated arms (immediate antiretroviral treatment and after 2 months of TB treatment). It is not surprising then that this prospective study in Thailand found that TB patients who took antiretroviral treatment had one-fifth the risk of dying as those who did not and those who started antiretroviral treatment earlier did better. Physicians need to overcome their concerns about overlapping toxicity, pill burden, and immune reconstitution inflammatory syndrome to place all their TB/HIV infected patients on cotrimoxazole and those with CD4+ counts under 350 cells on antiretroviral treatment.**

6. Health care delivery

Kiggundu V, Watya S, Kigozi G, Serwadda D, Nalugoda F, Buwembo D, Settuba A, Anyokorit M, Nkale J, Kighoma N, Ssempijja V, Wawer M, Gray RH. The number of procedures required to achieve optimal competency with male circumcision: findings from a randomized trial in Rakai, Uganda. *BJU Int.* 2009 Apr 17. [Epub ahead of print]

Kiggundu and colleagues set out to assess the number of procedures required to achieve optimal competency (time required for surgery with minimal adverse events) in Rakai, Uganda, and thus facilitate the development of guidelines for training providers, as male circumcision reduces the acquisition of human immunodeficiency virus (HIV) in men and is recommended for HIV prevention. In a randomized trial, 3011 men were circumcised, using the sleeve method, by six physicians who had completed training, which included 15-20 supervised procedures. The duration of surgery from local anaesthesia to wound closure, moderate or severe surgery-related adverse events, and wound healing were assessed in relation to the number of procedures done by each physician. The median age of the patients was 24 years. The number of procedures per surgeon was 20-981. The mean time required to complete surgery was approximately 40 min for the first 100 procedures and declined to 25 min for the subsequent 100 circumcisions. After controlling for the number of procedures there was no significant difference in duration of the surgery by patient HIV status or age. The rate of moderate and severe adverse events was 8.8% (10/114) for the first 19 unsupervised procedures after training, 4.0% for the next 20-99 (13/328) and 2.0% for the last 100 (P for trend, 0.003). All adverse events resolved with management. The completion

of more than 100 circumcisions was required before newly trained physicians achieved the optimum duration of surgery. Adverse events were higher immediately after training and additional supervision is needed for at least the first 20 procedures after completing training. **Editors' note: This is the kind of operational research that will improve service outcomes if its results are now taken on board. They strongly suggest that time pressure should not be placed on newly trained surgeons, who will become more efficient with time in any case, and that they should be supervised for the first 20 circumcisions they perform after training, in addition to periodic supervision for the next 80. This surgical procedure, described in male circumcision circles as 'minor surgery on a major organ', warrants the strong emphasis being placed on safety and quality assurance.**

Kline MW, Ferris MG, Jones DC, Calles NR, Mizwa MB, Schwarzwald HL, Wanless RS, Schutze GE. The Paediatric AIDS Corps: responding to the African HIV/AIDS health professional resource crisis. *Paediatrics*. 2009 Jan;123(1):134-6.

Health professional capacity for delivery of HIV care and treatment is severely constrained across sub-Saharan Africa. African health professional expertise in paediatrics is in particularly short supply. Here Kline et al describe a Paediatric AIDS Corps program that was designed to place paediatricians and other physicians in Africa on a long-term basis to expand existing health professional capacity for paediatric and family HIV care and treatment. In the first 2 years of this program, 76 physicians were placed in 5 African countries that have been hit hard by AIDS. Enrolment of HIV-infected children in care more than quadrupled over a 24-month period, to 26 590. The authors believe that this pilot program can serve as a model for larger-scale efforts to immediately expand access for African children and families to life-saving HIV care and treatment. **Editors' notes: With health professional capacity for delivering HIV treatment and care severely constrained across sub-Saharan Africa, attention has turned to task-shifting to other health cadres, task-sharing which involves parts of procedures or tasks being taken on by different health care providers, recruiting and retaining new health caregivers, and hosting short-term volunteer projects. This programme, responding to the fact that children are underrepresented among patients on antiretroviral treatment in virtually every setting in sub-Saharan Africa, mobilised US graduates of residency training programmes in paediatrics, family medicine, and internal medicine for assignments of a year or longer in Botswana, Lesotho, Swaziland, Malawi, and Burkina Faso. They receive a living stipend, full benefits, a housing allowance, and student loan debt relief. The programme plans its own obsolescence by training local health professionals. Its success in improving paediatric treatment coverage while being locally acceptable will be of interest to many worldwide who would like to contribute in some way to improve the dire situation of the vast majority of the 2 million children living with HIV in Africa.**

Kim JC, Askew I, Muvhango L, Dwane N, Abramsky T, Jan S, Ntlemo E, Chege J, Watts C. RADAR, School of Public Health, University of the Witwatersrand, Acornhoek, South Africa. Comprehensive care and HIV prophylaxis after sexual assault in rural South Africa: the Refentse intervention study. *BMJ*. 2009 Mar 13;338:b515.

Although international guidelines specify the central role of the health sector in providing comprehensive care, including HIV post-exposure prophylaxis (PEP), after sexual assault, in both industrialised and developing countries there are many challenges to providing timely and comprehensive services. A nurse-driven model of post-rape care was integrated into existing hospital services; the before and after study design evaluated impacts on quality of

care, reviewing 334 hospital charts and conducting interviews with 16 service providers and 109 patients in a 450-bed district hospital in rural South Africa. The key measures for improvement examined were quality of care after rape (forensic history and examination, provision of emergency contraception, prophylaxis for sexually transmitted infections, referrals); provision of HIV counselling and testing and provision and completion of full 28 day course of PEP; and service utilisation (number of service providers seen on first visit and number of rape cases presenting to hospital per month). After completing baseline research, Kim and colleagues introduced a five-part intervention model, consisting of a sexual violence advisory committee, hospital rape management policy, training workshop for service providers, designated examining room, and community awareness campaigns. Existing services had been fragmented and of poor quality. After the intervention, there were considerable improvements in clinical history and examination, pregnancy testing, emergency contraception, prophylaxis for sexually transmitted infections; HIV counselling and testing, PEP, trauma counselling, and referrals. Completion of the 28-day course of PEP drugs increased from 20% to 58%. The authors conclude that it is possible to improve the quality of care after sexual assault, including HIV prophylaxis, within a rural South African hospital at modest cost, using existing staff. With additional training, nurses can become the primary providers of this care. **Editors' note: Refentse means 'we shall overcome' in Venda, the language of this rural South African area and that is exactly what these investigators aimed to do. Aside from immediate genital and bodily injuries, sexual violence brings risks of HIV and sexually transmitted disease, unwanted pregnancy, urinary tract infections, chronic pelvic pain, miscarriage, depression, substance abuse, post-traumatic stress disorder, and suicide. They used formative research to conduct a baseline assessment with providers and patients to define problems and design a strategy for change. The process and its positive findings are an example for managers and providers of sexual assault care, but also of other services, who are keen to embark on a transparent, participatory process to improve their programme outcomes.**

7. Novel treatment approaches: gene therapy

Mitsuyasu RT, Merigan TC, Carr A, Zack JA, Winters MA, Workman C, Bloch M, Lalezari J, Becker S, Thornton L, Akil B, Khanlou H, Finlayson R, McFarlane R, Smith DE, Garsia R, Ma D, Law M, Murray JM, von Kalle C, Ely JA, Patino SM, Knop AE, Wong P, Todd AV, Haughton M, Fuery C, Macpherson JL, Symonds GP, Evans LA, Pond SM, Cooper DA. Phase 2 gene therapy trial of an anti-HIV ribozyme in autologous CD34(+) cells. *Nat Med.* 2009 Mar;15(3):285-92. Gene transfer has potential as a once-only treatment that reduces viral load, preserves the immune system, and avoids lifetime highly active antiretroviral therapy. This study, which is to the knowledge of Mitsuyasu and colleagues the first randomized, double-blind, placebo-controlled, phase 2 cell-delivered gene transfer clinical trial, was conducted in 74 HIV-1-infected adults who received a tat-vpr-specific anti-HIV ribozyme (OZ1) or placebo delivered in autologous CD34(+) hematopoietic progenitor cells. There were no OZ1-related adverse events. There was no statistically significant difference in viral load between the OZ1 and placebo group at the primary end point (average at weeks 47 and 48), but time-weighted areas under the curve from weeks 40-48 and 40-100 were significantly lower in the OZ1 group. Throughout the 100 weeks, CD4(+) lymphocyte counts were higher in the OZ1 group. This study indicates that cell-delivered gene transfer is safe and biologically active in individuals with HIV and can be developed as a conventional therapeutic product. **Editors' note: Gene therapy, which could prove a long-lived alternate to small molecule**

antiretroviral therapy, includes a variety of approaches. Ribozymes, used in this Phase II trial, are catalytic RNA molecules that can be engineered to target specific RNA sequences without 'off target' effects. These investigators hypothesized that a tat-vpr-specific anti-HIV ribozyme would make immune cell forbears change to produce a pool of mature bone marrow and lymph cells that would be protected from HIV replication. Although the trial did not show efficacy, viral loads were consistently lower in the treated group and there were no safety concerns. These are early days for gene therapy for HIV infection but initial results hold some promise.

8. *Workplace responses*

Van der Borgh SF, Clevenbergh P, Rijckborst H, Nsalou P, Onyia N, Lange JM, de Wit TF, Van der Loeff MF. Mortality and morbidity among HIV type-1-infected patients during the first 5 years of a multicountry HIV workplace programme in Africa. *Antivir Ther.* 2009;14(1):63-74.

Van der Borgh and colleagues aimed to evaluate the effectiveness of an HIV workplace programme in sub-Saharan Africa. The international brewing company, Heineken, introduced an HIV workplace programme in its African subsidiaries in 2001. Beneficiaries from 16 sites in 5 countries were eligible. HIV type-1 (HIV-1)-infected individuals were assessed clinically and immunologically, and started highly active antiretroviral therapy if they had AIDS or had a CD4+ T-cell count <300 cells/microl. In this cohort, study patients were followed-up for vital status, new AIDS events, CD4+ T-cell count, and haemoglobin. Over the first 5 years of the programme, 431 adults were found to be HIV-1-infected. The mortality rate among those not yet taking highly active antiretroviral therapy was 2.6 per 100 person-years of observation. By October 2006, 249 patients had started highly active antiretroviral therapy at a median CD4+ T-cell count of 170 cells/microl; 59 (23.7%) patients were in CDC stage C. Among patients on highly active antiretroviral therapy, 25 died and 7 were lost to follow-up. The mortality rate was 3.7 per 100 person-years of observation overall, 14 per 100 person-years of observation in the first 16 weeks and 2.5 per 100 person-years of observation thereafter (P < 0.0001). At 4 years after start of treatment, 89% of patients were known to be alive. The CD4+ T-cell count increased by a median of 153 and 238 cells/microl after 1 and 4 years of highly active antiretroviral therapy, respectively. In this HIV workplace programme in sub-Saharan Africa, long-term high survival was achieved. **Editors' note: Leading the way forward for private sector engagement in HIV in Africa, this private sector company began implementing an HIV workplace programme in May 2001 in Nigeria, Rwanda, Burundi, Republic of Congo, and Democratic Republic of Congo. Not only its own direct staff but also the African staffs of its subsidiaries, their spouses, and their children are entitled to free healthcare by the company. With voluntary and confidential HIV testing, assessment for treatment initiation, no drug stock-outs, and good treatment durability with low loss to follow-up, this small but well-managed and adequately funded programme achieved excellent treatment outcomes over 5 years. This is a good example of corporate social responsibility in action - cheers!**

9. *HIV transmission on antiretroviral treatment*

Attia S, Egger M, Müller M, Zwahlen M, Low N. Sexual transmission of HIV according to viral load and antiretroviral therapy: systematic review and meta-analysis. *AIDS.* 2009 Apr 17. [Epub ahead of print]

Attia and colleagues aimed to synthesize the evidence on the risk of HIV transmission through unprotected sexual intercourse according to viral load and treatment with

combination antiretroviral therapy. They conducted a systematic review and meta-analysis, searching Medline, Embase, and conference abstracts from 1996-2009. The authors included longitudinal studies of serodiscordant couples reporting on HIV transmission according to plasma viral load or use of antiretroviral therapy and used random-effects Poisson regression models to obtain summary transmission rates [with 95% confidence intervals, (CI)]. If there were no transmission events they estimated an upper 97.5% confidence limit. They identified 11 cohorts reporting on 5021 heterosexual couples and 461 HIV-transmission events. The rate of transmission overall from antiretroviral therapy-treated patients was 0.46 (95% CI 0.19-1.09) per 100 person-years, based on five events. The transmission rate from a seropositive partner with viral load below 400 copies/ml on antiretroviral therapy, based on two studies, was zero with an upper 97.5% confidence limit of 1.27 per 100 person-years, and 0.16 (95% CI 0.02-1.13) per 100 person-years if not on antiretroviral therapy, based on five studies and one event. There were insufficient data to calculate rates according to the presence or absence of sexually transmitted infections, condom use, or vaginal or anal intercourse. Studies of heterosexual discordant couples observed no transmission in patients treated with antiretroviral therapy and with viral load below 400 copies/ml, but data were compatible with one transmission per 79 person-years. Further studies are needed to better define the risk of HIV transmission from patients on antiretroviral therapy. **Editors' note: This study underscores the considerable uncertainty about the risk of HIV transmission under 'Swiss Commission' conditions, that is, viral load below 40 copies/ml, no other sexually transmitted infection, and consistent adherence to antiretroviral treatment. The Commission stated 'much lower than one per 100,000 acts of sexual intercourse' whereas this systematic review and meta-analysis of existing data found them compatible with one new infection for every 79 person-years of follow-up (or 7900 acts of sexual intercourse, if the yearly average is 100 contacts). Further studies are needed to quantify HIV transmission risk in different populations, including men who have sex with men for whom there are no comparable published data. In the meantime, since the Swiss Commission statement January 2008 UNAIDS has continued to reassert the importance of correct and consistent condom use - a key part of positive prevention and a cornerstone of HIV prevention for people without HIV.**

Wood E, Kerr T, Marshall BD, Li K, Zhang R, Hogg RS, Harrigan PR, Montaner JS. Longitudinal community plasma HIV-1 RNA concentrations and incidence of HIV-1 among injecting drug users: prospective cohort study. *BMJ*. 2009 Apr 30;338:b1649.

To examine the relation between plasma HIV-1 RNA concentrations in the community and HIV incidence among injecting drug users, Wood and colleagues conducted a prospective cohort study in an inner city community in Vancouver, Canada. Injecting drug users, with and without HIV, were followed up every six months between 1 May 1996 and 30 June 2007. The main outcome measures were estimated community plasma HIV-1 RNA in the six months before each HIV-negative participant's follow-up visit and associated HIV incidence. Among 622 injecting drug users with HIV, 12 435 measurements of plasma HIV-1 RNA were obtained. Among 1429 injecting drug users without HIV, there were 155 HIV seroconversions, resulting in an incidence density of 2.49 (95% confidence interval 2.09 to 2.88) per 100 person years. In a Cox model that adjusted for unsafe sexual behaviours and using nonsterile syringes, the estimated community plasma HIV-1 RNA concentration remained independently associated with the time to HIV seroconversion (hazard ratio 3.32 (1.82 to 6.08, P<0.001), per log(10) increase). When the follow-up period was limited to

observations after 1 January 1998 (when the median plasma HIV RNA concentration was <20 000 copies/ml), the median viral load was no longer statistically associated with HIV incidence (1.70 (0.79 to 3.67, P=0.175), per log(10) increase). The authors concluded that a longitudinal measure of community plasma HIV-1 RNA concentration was correlated with the community HIV incidence rate and predicted HIV incidence independent of unsafe sexual behaviours and sharing used syringes. If these findings are confirmed, they could help to inform both HIV prevention and treatment interventions. **Editors' note: This ecological study estimated community plasma viral load from the viral loads of injecting drug users on treatment in this urban community which has a centralised antiretroviral dispensation programme and HIV laboratory. The proportion of patients on 3 or more antiretroviral drugs increased from 8.4% in 1996 to 98.8% in 2007 while both median estimated community plasma HIV-1 RNA concentrations and HIV incidence fell. The likelihood that an HIV-negative injecting drug user had seroconverted since the last clinic visit was correlated with the median estimated community viral load during the prior 6 months. It is not possible to conclude from these data that the association was causal but the fact that the highest rates of HIV seroconversion occurred in the year after the highest community plasma HIV-2 concentration support this hypothesis. These findings no doubt influenced the provincial government to fund an innovative programme to expand access to treatment for street-involved people living in Vancouver's downtown eastside and downtown Prince George, British Columbia.**

10. Communications

Winskell K, Enger D. A new way of perceiving the pandemic: the findings from a participatory research process on young Africans' stories about HIV/AIDS. *Cult Health Sex*. 2009 May;11(4):453-67.

This paper presents the findings, shares the methodology, and outlines the benefits of a multi-country participatory research process on a unique data source: stories about HIV and AIDS written by young Africans. Between 1997 and 2005, more than 105,000 young people from 37 countries participated in competitions inviting them to think up storylines for short fiction films to educate their communities about HIV as part of the 'Scenarios from Africa' communication process. The winning stories were selected by juries made up of people living with HIV and other local specialists in prevention, treatment and care; former contest winners and other young people; and communication specialists, including the top African directors, who went on to transform the ideas into short films. In 2005, over 200 jurors selected 30 winners from the 22,894 stories submitted that year by 63,327 contest participants. After reading around 200 stories each and participating in the selection process, jurors compiled their observations and recommendations. The jurors' findings reveal notable persistent shortcomings in existing communication efforts and identify key emerging needs. In some areas, they show remarkable consistency across the continent. Jurors view this as a powerful needs assessment, networking, and capacity building process that motivates action. **Editors' note: Between 1997 and 2005 the Scenarios in Africa participatory communication initiative ran four contest cycles for storylines for short fiction films, producing an average of three films a year by Africa's most celebrated filmmakers (viewable at www.globaldialogues.org) to trigger discussion about the epidemic in communities across West Africa. Analysis of 2005 submissions revealed a high level of understanding of basic facts, most marked among younger contestants. The most common recommendation made by the jurors was for destigmatisation to counter**

moralisation of the epidemic and to humanise people living with HIV. Jurors placed primary emphasis on fostering the life skills of young people so they can enact HIV prevention. Mobilised to submit stories by more than 1000 local organisations, the participating young people communicated rich insight into their contextualised understanding of the epidemic, information from the front lines of youth prevention in Africa with direct relevance for creating more enabling environments for HIV prevention.

11. Blood donor referral

Vamvakas EC. Scientific background on the risk engendered by reducing the lifetime blood donation deferral period for men who have sex with men. *Transfus Med Rev.* 2009 Apr;23(2):85-102.

The lifetime deferral for men who have sex with men has not been harmonized with the 12-month deferral for similar-risk activities through heterosexual contacts. This occurs primarily because of fears of increased transfusion transmission of known sexually and transfusion-transmitted viruses for which donor blood is (eg, HIV) or is not (eg, human herpesvirus 8 [HHV-8]) tested and also of fears of novel agents that may share the epidemiology and long asymptomatic phase of HIV. A 12-month men who have sex with men deferral could result in release of 1 HIV-infectious donation every 11 years in the United States. This risk is smaller than the risk from allowing the continued use of pooled whole blood-derived platelets (release of 1 infectious platelet dose every 1.67 years), a risk that is considered "tolerable." Provided that measures to reduce the number of allogeneic-donor exposures to novel pathogens (which may be vector- or food-borne rather than sexually transmitted) are implemented, and the deferral for similar-risk activities through heterosexual contacts is extended to 5 years, a 5-year men who have sex with men deferral could be justified because of the interval between emergence of a novel pathogen and introduction of measures to protect the blood supply. Also, provided that measures to protect the blood supply from HHV-8 are implemented, a lifetime men who have sex with men deferral could be justified because of the uncertainty about the clinical consequences of transfusion transmission of HHV-8. Because such alternate measures, which would have had a greater impact on safety than the men who have sex with men deferral, have not been implemented to demonstrate a consistent approach to safety, maintenance of the current men who have sex with men deferral appears to be selectively precautionary and cannot be justified. **Editors' note: Arguments have been advanced to harmonise the deferral periods for men who have sex with men with those for heterosexuals with similar-risk activities. Argentina, Brazil, Japan, Hungary, New Zealand, Russia, and South Africa have substituted a 1-, 5-, or 10-year deferral for the lifetime deferral of men who have sex with men. The USA, Canada, and the 19-nation European Blood Alliance maintain their current positions. This article argues cogently for a scientifically based, consistent approach to blood safety. It highlights the ramifications for blood safety of inconsistencies in national policies, arguing that the men who have sex with men lifetime deferral is selectively precautionary. More can be achieved by interventions to protect the blood supply against HHV-8 and by prohibiting the use of pooled whole blood-derived platelets. On balance, arguments can be made that extending the heterosexual deferral from 1 year to 5 years and harmonising the men who have sex with men deferral to 5 years would reasonably protect against an 'HIV-like' agent that could emerge in the future.**

12. Human Rights

Amon JJ, Kasambala T. Structural barriers and human rights related to HIV prevention and treatment in Zimbabwe. *Glob Public Health*. 2009 Mar 26:1-17. [Epub ahead of print]

There has long been recognition that individual risk factors can only partially explain vulnerability to HIV infection, and that a broader range of socioeconomic, cultural and political factors must be taken into account. More recently this understanding has been applied to addressing obstacles to accessing HIV treatment. Yet, while structural interventions aimed at contextual factors related to HIV prevention and treatment have been shown to be effective, they have not been widely implemented. Using the situation of Zimbabwe as an example, Amon and Kasambala present an illustration of how contextual barriers can be understood in human rights terms, and how using a human rights analysis can specifically help define 'structural-rights' interventions and compel their implementation.

Editors' note: This article, a must-read for all those interested in effective combination prevention, demonstrates how explicitly recognising human rights provides a mechanism to address structural level barriers to HIV prevention and care, reinforcing government and donor agency accountability to redress societal power differentials. In other words, situating concerns about the socioeconomic, cultural, and political barriers to HIV prevention within a context of human rights provides a framework for action founded on the obligations and responsibilities of states. Drawing on the current HIV and human rights crisis in Zimbabwe, specific examples are provided of concrete structural-rights interventions to address the right to earn a livelihood and own property; the right to freedom of expression, assembly, and information; the right to freedom from gender-based and sexual violence; and the right to the progressive realisation of health.

That was *HIV this week*, signing off.

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