Welcome to the 74th issue of HIV This Week! In this issue we cover these topics:

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   • Why investing in vaccine research holds promise in the United States

2. Paediatric HIV testing
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   • Zambia reports excellent results of a routine offer of HIV counselling to caregivers and HIV testing for hospitalized paediatric patients

3. Masculinity and risk
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    • South African kids having been starting sex at the same age for years but HIV has become a bed partner. What needs to be done?

Cate Hankins  Brian Houle  Tania Lemay  Precious Lunga  Paul Morejon
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Don’t forget that you can find a wealth of information on the HIV epidemic and responses to it at www.unaids.org.
1. Biomedical interventions: vaccines

Vaccination with ALVAC and AIDSVAX to Prevent HIV-1 Infection in Thailand.


The development of a safe and effective vaccine against the human immunodeficiency virus type 1 (HIV-1) is critical to pandemic control. In a community-based, randomized, multicenter, double-blind, placebo-controlled efficacy trial, the authors evaluated four priming injections of a recombinant canarypox vector vaccine (ALVAC-HIV [vCP1521]) plus two booster injections of a recombinant glycoprotein 120 subunit vaccine (AIDSVAX B/E). The vaccine and placebo injections were administered to 16,402 healthy men and women between the ages of 18 and 30 years in Rayong and Chon Buri provinces in Thailand. The volunteers, primarily at heterosexual risk for HIV infection, were monitored for the coprimary end points: HIV-1 infection and early HIV-1 viraemia, at the end of the 6-month vaccination series and every 6 months thereafter for 3 years. In the intention-to-treat analysis involving 16,402 subjects, there was a trend toward the prevention of HIV-1 infection among the vaccine recipients, with a vaccine efficacy of 26.4% (95% confidence interval [CI], –4.0 to 47.9; P=0.08). In the per-protocol analysis involving 12,452 subjects, the vaccine efficacy was 26.2% (95% CI, –13.3 to 51.9; P=0.16). In the modified intention-to-treat analysis involving 16,395 subjects (with the exclusion of 7 subjects who were found to have had HIV-1 infection at baseline), the vaccine efficacy was 31.2% (95% CI, 1.1 to 51.2; P=0.04). Vaccination did not affect the degree of viraemia or the CD4+ T-cell count in subjects in whom HIV-1 infection was subsequently diagnosed. This ALVAC-HIV and AIDSVAX B/E vaccine regimen may reduce the risk of HIV infection in a community-based population with largely heterosexual risk. Vaccination did not affect the viral load or CD4+ count in subjects with HIV infection. Although the results show only a modest benefit, they offer insight for future research.

For access to abstract click here: 1

Editors' note: These encouraging results are sparking HIV vaccine scientists to explore how this prime-boost strategy using vaccines that were adapted to circulating Thai subtypes (B and E) provided modest levels of protection. This paper was published on line October 20th simultaneously with the plenary presentation of the results at the AIDS Vaccine 2009 conference in Paris. Webcasting of the conference sessions and media conferences, including the RV144 media conference, is available to viewers until January 21, 2010 at 12:00 PM Central European Time at: http://www.hivvaccineenterprise.org/conference/2009/webcasting.html The mITT or modified intent-to-treat analysis is the gold standard analysis that was followed by the trial’s Data Safety Monitoring Board throughout this test-of-concept trial. It includes all trial participants randomised in the trial with the exception of 7 who were already HIV infected at their first post-screening study visit before the first shot. How exactly did this strategy work (what are the immune correlates of protection?), how high did vaccine efficacy go in the first year and how much did it decrease after the first year post-vaccination (would booster doses be needed?), does the vaccine work better in those at lower risk of infection (why and what would that mean for future vaccine trial design?), was it a single vaccine or the prime-boost combination that produced protective immune responses, was matching the vaccines to Thai virus subtypes important to vaccine efficacy in this study population, and are there different immune system responses to prevent HIV infection compared to those that attempt to control it after infection is established? These and many other intriguing questions are opening up avenues for exploration and invigorating us all. An HIV vaccine is many years away but now we know that it will come.
Potential population health outcomes and expenditures of HIV vaccination strategies in the United States.

Long EF, Brandeau ML, Owens DK. Vaccine. 2009; 27(5402-5010).

Estimating the potential health benefits and expenditures of a partially effective HIV vaccine is an important consideration in the debate about whether HIV vaccine research should continue. We developed an epidemic model to estimate HIV prevalence, new infections, and the cost-effectiveness of vaccination strategies in the U.S. Vaccines with modest efficacy could prevent 300,000-700,000 HIV infections and save $30 billion in healthcare expenditures over 20 years. Targeted vaccination of high-risk individuals is economically efficient, but difficulty in reaching these groups may mitigate these benefits. Universal vaccination is cost-effective for vaccines with 50% efficacy and price similar to other infectious disease vaccines.

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Editors’ note: This is the first analysis to estimate quantitatively the potential health and economic outcomes of a targeted or a universal HIV vaccination programme in the USA, where its estimated that 1.3 million new infections will occur over the next 20 years. Under a variety of scenarios and assumptions about vaccine efficacy and epidemic dynamics in the late-stage US epidemic, investment in vaccines results in positive health and economic outcomes, being ‘good value for money’. These models can be further refined, as we learn more about vaccine efficacy by mode of transmission and intensity of HIV exposure, and then applied to low- and middle-income countries where 40 million new infections are expected to occur over the next 20 years.

2. Paediatric HIV testing

Universal HIV testing of infants at immunization clinics: an acceptable and feasible approach for early infant diagnosis in high HIV prevalence settings.


Rollins and colleagues set out to determine the acceptability and feasibility of universal HIV testing of 6-week-old infants attending immunization clinics to achieve early diagnosis of HIV and referral for HIV treatment and care services. The study design was an observational cohort within which routine HIV testing of infants was offered to all mothers bringing infants for immunizations at three clinics in KwaZulu Natal. Blood samples were collected by heel prick onto filter paper. Dried blood spots were tested for HIV antibodies and, if present, were tested for HIV DNA by PCR. Exit interviews were requested of all mothers irrespective of whether they had agreed to infant testing or not. Of 646 mothers bringing infants for immunizations, 584 (90.4%) agreed to HIV testing of their infant and 332 (56.8%) subsequently returned for results. Three hundred and thirty-two of 646 (51.4%) mothers and infants thereby had their HIV status confirmed or reaffirmed by the time the infant was 3 months of age. Overall, 247 of 584 (42.3%) infant dried blood spot samples had HIV antibodies indicating maternal HIV status. Of these, 54 (21.9%) samples were positive for HIV DNA by PCR. This equates to 9.2% (54/584) of all infants tested. The majority of mothers interviewed said they were comfortable with testing of their infant at immunization clinics and would recommend it to others. Screening of all infants at immunization clinics is acceptable and feasible as a means for early identification of HIV-infected infants and referral for antiretroviral therapy.

For access to abstract click here: _1_
Routine offering of HIV testing to hospitalized paediatric patients at university teaching hospital, Lusaka, Zambia: acceptability and feasibility.


The difficulties diagnosing infants and children with HIV infection have been cited as barriers to increasing the number of children receiving antiretroviral therapy worldwide. Kankasa and colleagues implemented routine HIV antibody counselling and testing for paediatric patients hospitalized at the University Teaching Hospital, a national reference centre, in Lusaka, Zambia. They also introduced HIV DNA polymerase chain reaction testing for early infant diagnosis.

Caregivers/parents of children admitted to the hospital wards were routinely offered HIV counselling and testing for their children. HIV antibody positive (HIV+) children <18 months of age were tested with PCR for HIV DNA. From January 1, 2006, to June 30, 2007, among 15,670 children with unknown HIV status, 13,239 (84.5%) received counselling and 11,571 (87.4%) of those counselled were tested. Overall, 3373 (29.2%) of those tested were seropositive. Seropositivity was associated with younger age: 69.6% of those testing HIV antibody positive were <18 months of age. The proportion of counselled children who were tested increased each quarter from 76.0% in January to March 2006 to 88.2% in April to June 2007 (P < 0.001). From April 2006 to June 2007, 1276 polymerase chain reaction tests were done; 806 (63.2%) were positive. The rate of PCR positivity increased with age from 22% in children <6 weeks of age to 61% at 3-6 months and to 85% at 12-18 months (P < 0.001). Routine counselling and offers of antibody testing of paediatric inpatients can identify large numbers of HIV-seropositive children in high prevalence settings. The high rate of HIV infection in hospitalized infants and young children also underscores the urgent need for early infant diagnostic capacity in high prevalence settings.

Editors’ note: Globally, the number of children under 15 years of age who received antiretroviral treatment rose from 198,000 in 2007 to 275,000 in 2008; however, a striking 62% of children in low- and middle-income countries who need antiretroviral treatment are not receiving it. Among the many barriers to overcome in the scale-up of paediatric HIV treatment to universal access, the major gatekeeper is identifying children with HIV infection. Before the study began in this Lusaka referral hospital, children were sent to adjacent voluntary testing and counselling centres for determination of serostatus. The uptake of paediatric testing among caregivers that were counselled on the wards increased over time to an overall 87%. The result was that 29% of the children tested were found to be HIV-antibody positive, 63% of whom were infected. There is no doubt that referral hospitals in high HIV prevalence countries can increase paediatric-testing uptake dramatically if HIV counselling and testing are offered routinely at the point of care.

3. Masculinity and risk

Questioning gender norms with men to improve health outcomes: Evidence of impact.

This article describes a review of 58 evaluation studies of programmes with men and boys in sexual and reproductive health (including HIV prevention, treatment, care and support); father involvement; gender-based violence; maternal, newborn and child health; and gender socialisation.
more broadly. While few of the programmes go beyond the pilot stage, or a relatively short-term timeframe, they offer compelling evidence that **well-designed programmes with men and boys can lead to positive changes in their behaviours and attitudes** related to sexual and reproductive health; maternal, newborn and child health; their interaction with their children; their use of violence against women; their questioning of violence with other men; and their health-seeking behaviour. The evidence indicates that programmes that incorporate a **gender-transformative approach** and **promote gender-equitable relationships** between men and women are more effective in producing behaviour change than narrowly focused interventions, as are programmes which reach beyond the individual level to the social context.

**Editors’ note:** Gender norms are the social expectations of appropriate roles and behaviours for men and women. They vary across historical and local economic, religious, and cultural contexts and are created and reinforced by families, communities, and social/political/legal environments. Because gender norms are learned and internalized, rather than being biologically determined, they can also be questioned and transformed to be more gender-equitable. This review confirms that comprehensive programmes with men and boys that include specific discussions about the social meanings of men and masculinity seem to show the highest levels of effectiveness. More research is needed to assess the impact of public policy changes and social trends on the behaviour of men and boys, on the bidirectional expectations of both sexes, and on early and potentially gender-transformative practices in men’s involvement as fathers.

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**Intimate Partner Violence Perpetration, Standard and Gendered STI/HIV Risk Behaviour, and STI/HIV Diagnosis Among A Clinic-Based Sample of Men.**


The estimated one in three women worldwide victimized by intimate partner violence consistently demonstrate elevated STI/HIV prevalence; abusive male partners’ risky sexual behaviours and subsequent infection are implicated. Little empirical data exist to characterize men’s sexual risk as it relates to violence perpetration and STI/HIV. **Data from a survey of men aged 18-35 recruited from three community-based health clinics in an urban area (n=1585) were analyzed to assess the prevalence of intimate partner violence perpetration and relations of such violent behaviour with both standard (e.g., anal sex, injection drug use) and gendered (e.g., coercive condom practices, sexual infidelity) forms of sexual risk, and STI/HIV diagnosis.** Approximately one third of participants (32.7%) reported perpetrating violence against an intimate partner in their lifetime; 1 in 8 (12.4%) participants reported history of STI/HIV diagnosis. Men’s intimate partner violence perpetration related to both standard and gendered STI/HIV risk behaviours (AORS 1.72 to 6.22) and to STI/HIV diagnosis (OR 4.85, 95% CI 3.54, 6.66). In a multivariate model, the association of men’s intimate partner violence perpetration with STI/HIV diagnosis was partially attenuated (AOR 2.55, 95% CI 1.77, 3.67), and an independent association of gendered sexual risk behaviours were found to be independently related to STI/HIV diagnosis. Men’s perpetration of violence against intimate partners is common among this population. Abusive men are at increased risk for STI/HIV, with gendered forms of sexual risk behaviour partially responsible. Findings indicate the need for interwoven sexual health promotion and violence prevention efforts targeted to men that include addressing gendered sexual risk.

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**Editors’ note:** In this cross-sectional US study of young, urban, adult men attending community health centres, a third of participants reported having perpetrated physical or sexual violence against an intimate partner. Multivariate analysis found an independent association between a history or such violence and gendered STI/HIV risk (e.g. sexual infidelity, coercive condom practices). Programmes that integrate men’s prevention of intimate partner violence into STI/HIV prevention should focus on modifying masculinity norms that support men’s entitlement to sexual control of women because these attitudes underpin both intimate partner violence and sexual risk behaviour.
4. Foreskin inflammation

Foreskin inflammation is associated with HIV and herpes simplex virus type-2 infections in Rakai, Uganda.


Johnson and colleagues assessed foreskin inflammation associated with HIV and herpes simplex virus type 2 (HSV-2) in circumcised men. Foreskin tissues were assessed in 97 HIV-infected and 135 HIV-uninfected men enrolled in randomized trials of circumcision in Rakai, Uganda. Inflammation was quantified using an ordinal score evaluating extent, intensity, and cellular composition of infiltrates in the epithelium and stroma. Prevalence rate ratios of inflammation were estimated by multivariate Poisson regression. Foreskin inflammation was primarily focal. Epithelial inflammation was present in 4.2% of men with neither HIV nor HSV-2 infection; 7.8% of men with only HSV-2; 19.0% with HIV alone (P = 0.04); and 31.6% in HIV/HSV-2 coinfected men [prevalence rate ratio (PRR) 7.5, 95% confidence interval (CI) 2.3-23.8, P < 0.001]. Stromal inflammation was present in 14.1% of HIV/HSV-2 uninfected men, compared with 29.7% in men with HSV-2 alone (P = 0.03), 33.3% in men with HIV alone (P = 0.04), and 61.0% in men with HIV/HSV-2 co-infection (PRR 4.3, 95% CI 2.3-7.9, P < 0.001). In HIV-infected men, epithelial inflammation was associated with higher HIV viral load. **Epithelial inflammation was more frequent among men reporting recent genital ulceration. Both epithelial and stromal inflammation were more common among men with smegma on physical examination. Foreskin inflammation is increased with HIV and HSV-2 infections, higher HIV viral load and presence of smegma.** Foreskin inflammation may have implications for HIV transmission and acquisition in uncircumcised men.

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Editors’ note: This analysis of foreskins removed at medical circumcision supports the idea that local mucosal inflammation and ulcerative lesions, as well as recruitment of lymphocytes that target HIV to genital tissues, can influence HIV susceptibility and infectivity. Causative links cannot be made because this is a cross-sectional study but the highest prevalence of foreskin inflammation (in the epithelium and in the layer below it), was found in men with HIV/HSV-2 co-infection. Inflammation was also associated with smegma, a possible surrogate marker of poor genital hygiene. Since smegma could be the result of local inflammation or it be contributing to it, further research is warranted.

5. Health systems and human resources for health

The effects of global health initiatives on country health systems: a review of the evidence from HIV/AIDS control.


This paper reviews country-level evidence about the impact of global health initiatives, which have had profound effects on recipient country health systems in middle- and low-income countries. Biesma and colleagues have selected three initiatives that account for an estimated **two-thirds of external funding earmarked for HIV control in resource-poor countries:** the Global Fund to Fight AIDS, TB and Malaria, the World Bank Multi-country AIDS Program (MAP) and the US President’s Emergency Plan for AIDS Relief (PEPFAR). This paper draws on 31 original country-specific and cross-country articles and reports, based on country-level fieldwork conducted between 2002 and 2007. **Positive effects have included a rapid scale-up in HIV service delivery, greater stakeholder participation, and channelling of funds to non-governmental stakeholders, mainly NGOs and faith-based bodies. Negative effects include**
**distortion of recipient countries’ national policies**, notably through distracting governments from coordinated efforts to strengthen health systems and **re-verticalization of planning, management and monitoring and evaluation systems**. Sub-national and district studies are needed to assess the degree to which global health initiatives are learning to align with and build the capacities of countries to respond to HIV; whether marginalized populations access and benefit from global health initiatives-funded programmes; and about the cost-effectiveness and long-term sustainability of the HIV programmes funded by the global health initiatives. Three multi-country sets of evaluations, which will be reporting in 2009, will answer some of these questions.

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**Editor’s note**:
Global health initiatives are defined as ‘a blueprint for financing, resourcing, coordinating and/or implementing disease control across at least several countries in more than one region of the world’. They may be bilateral (e.g. US PEPFAR), multilateral (e.g. World Bank MAP), or public-private partnerships (Global Fund) aid mechanisms. This first systematic review of published and unpublished reports from 2002 to 2007 examines the effects of these three initiatives on national policy; coordination and planning; stakeholder involvement; disbursement, absorptive capacity, and management; monitoring and evaluation; and human resources. It suggests that these initiatives, each with different effects, initially often had negative effects, revealing country system weaknesses. As lessons were learned, the effects on health systems were more positive. The principal recommendations of this review are first, that global health initiatives, recipient donor countries, civil society organisations, and technical agencies alike should engage more fully with the Paris Principles for AIDS Effectiveness. Secondly, country and global policy makers and donors should demand and fund the acquisition of better evidence, including more analytical health policy and health systems evaluation. This article should be very high on your reading list!

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**Task-shifting HIV counselling and testing services in Zambia: the role of lay counsellors**


The human resource shortage in Zambia is placing a heavy burden on the few health care workers available at health facilities. The Zambia Prevention, Care and Treatment Partnership began training and placing community volunteers as lay counsellors in order to complement the efforts of the health care workers in providing HIV counselling and testing services. These volunteers are trained using the standard national counselling and testing curriculum. This study was conducted to review the effectiveness of lay counsellors in addressing staff shortages and the provision of HIV counselling and testing services. Quantitative and qualitative data were collected by means of semistructured interviews from all active lay counsellors in each of the facilities and a facility manager or counselling supervisor overseeing counselling and testing services and clients. At each of the 10 selected facilities, all counselling and testing record books for the month of May 2007 were examined and any recordkeeping errors were tallied by cadre. Qualitative data were collected through focus group discussions with health care workers at each facility. **Lay counsellors provide counselling and testing services of quality and relieve the workload of overstretched health care workers.** Facility managers recognize and appreciate the services provided by lay counsellors. Lay counsellors provide up to 70% of counselling and testing services at health facilities. The data review revealed **lower error rates for lay counsellors, compared to health care workers, in completing the counselling and testing registers**. Community volunteers, with approved training and ongoing supervision, can play a major role at health facilities to provide counselling and testing services of quality, and relieve the burden on already overstretched health care workers.

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**Editors’ note**: Zambia is more than an order-of-magnitude (10 times) below the recommended staff-to-population ratios for nurses (1:700 versus 1:8064) and pharmacists (1:8000 versus
A two-week classroom component followed by a four-week supervised practicum and training in finger-prick HIV testing has created a cadre of lay counsellors providing quality services to satisfied clients. Some lay counsellors view reducing stigma and representing community role models as additional responsibilities. The fact that this is a voluntary programme (lay counsellors receive 25USD per month to defray travel costs but no other compensation) may jeopardise its sustainability. Continued supervision of the work of these lay counsellors, along with formalisation of their relationship with health facilities, could enhance both performance and retention.

6. Men who have sex with men

Prevalence of unprotected anal intercourse among HIV-diagnosed MSM who have sex with men in the United States: a meta-analysis.


Crepaz and colleagues set out to integrate the empirical findings on the prevalence of unprotected anal intercourse among HIV-diagnosed men who have sex with men in the United States by comprehensively searching MEDLINE, EMBASE, PsycINFO (2000-2007), hand searching bibliographic lists, and contacting researchers. Thirty US studies (n = 18 121) met selection criteria. Analyses were conducted using random-effects models and meta-regression. The prevalence of unprotected anal intercourse was considerably higher with HIV-seropositive partners (30%; 95% confidence interval 25-36) than with serostatus unknown (16%; 95% confidence interval 13-21) or HIV-seronegative partners (13%; 95% confidence interval 10-16). The prevalence of unprotected anal intercourse with either a serostatus unknown or HIV-seronegative partner was 26%. The unprotected anal intercourse prevalence did not differ by the length of the behavioural recall window but did vary by the type of anal intercourse (insertive vs. receptive). Studies with the following features had a lower unprotected anal intercourse prevalence: recruiting participants before 2000, men who have sex with men of colour being the majority of study sample, recruiting participants from medical settings, using random or systematic sampling methods, and having interviewers administer the questionnaire. Being on antiretroviral therapy, having an undetectable viral load, and reporting more than 90% medication adherence were not associated with unprotected anal intercourse. Most HIV-diagnosed men who have sex with men protect partners during sexual activity, but a sizeable percentage continues to engage in sexual behaviours that place others at risk for HIV infection and place themselves at risk for other sexually transmitted infections. Prevention with positives programs continues to be urgently needed for men who have sex with men in the United States.

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Editors’ note: Men who have sex with men who know their HIV-positive status may practice harm reduction approaches such as serosorting (only engaging in unprotected sex with seropositive partners) and strategic positioning (selectively engaging in unprotected receptive, rather than unprotected insertive anal intercourse because the per-act risk of transmission is lower. This meta-analysis quantitatively synthesized US literature, excluding studies recruiting male sex workers, methamphetamine users, and men with clinically diagnosed alcohol dependency, as well as those that recruited entirely from high-risk settings (gay brothels, sex parties, and barebacking websites). With the behavioural recall window ranging from last sex to the past 12 months (median 3 months), the study found no support for the hypothesis that clinical variables (treatment status, medication adherence, and viral load) were associated with unprotected anal intercourse. Rather, serosorting and strategic positioning appear to be intentional and deliberate HIV-related harm-reduction behaviours chosen by some HIV-positive men, The
relative safety of such strategies deserves urgent investigation given that there was a 26% increase in estimated male HIV cases among American men who have sex with men over the period 2004 to 2007. In 2007, 72% of male HIV cases from 38 US areas were attributed to male-to-male sexual activity.

High HIV Prevalence Among Men Who have Sex with Men in Soweto, South Africa: Results from the Soweto Men's Study.


The Soweto Men's Study assessed HIV prevalence and associated risk factors among men who have sex with men in Soweto, South Africa. Using respondent driven sampling recruitment methods, Lane and colleagues recruited 378 men who have sex with men (including 15 seeds) over 30 weeks in 2008. All results were adjusted for respondent driven sampling sampling design. Overall HIV prevalence was estimated at 13.2% (95% confidence interval 12.4-13.9%), with 33.9% among gay-identified men, 6.4% among bisexual-identified men, and 10.1% among straight-identified men who have sex with men. In multivariable analysis, HIV infection was associated with being older than 25 (adjusted odds ratio (AOR) 3.8, 95% CI 3.2-4.6), gay self-identification (AOR 2.3, 95% CI 1.8-3.0), monthly income less than ZAR500 (AOR 1.4, 95% CI 1.2-1.7), purchasing alcohol or drugs in exchange for sex with another man (AOR 3.9, 95% CI 3.2-4.7), reporting any URAI (AOR 4.4, 95% CI 3.5-5.7), reporting between six and nine partners in the prior 6 months (AOR 5.7, 95% CI 4.0-8.2), circumcision, (AOR 0.2, 95% CI 0.1-0.2), a regular female partner (AOR 0.2, 95% CI 0.2-0.3), smoking marijuana in the last 6 months (AOR 0.6, 95% CI 0.5-0.8), unprotected vaginal intercourse in the last 6 months (AOR 0.5, 95% CI 0.4-0.6), and STI symptoms in the last year (AOR 0.7, 95% CI 0.5-0.8). The results of the Soweto Men's Study confirm that men who have sex with men are at high risk for HIV infection, with gay men at highest risk. HIV prevention and treatment for men who have sex with men are urgently needed.

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Editors’ note: This is the first study of men who have sex with men in Africa to use respondent driven sampling (RDS) methodology to assess both HIV prevalence and risk factors. Intriguingly, the multivariate analysis revealed that the strongest adjusted odds ratio for associations with decreased risk of HIV infection was for being circumcised. Insertive anal intercourse was reported more commonly than receptive anal intercourse (85.2% ever versus 20.6% ever) and HIV prevalence among gay-identified men was more than 3 times that of bisexual and straight-identified men who have sex with men. Since the latter groups have to date been more likely to report the exclusive practice of insertive anal intercourse with male partners, this study may be providing the hypothesis-generating evidence that would support a trial of male circumcision for HIV prevention among primarily insertive men who have sex with men. On the more immediately practical side, rapid research is needed to find out whether current messages about male circumcision for HIV prevention are reaching bisexual and straight-identified men in South Africa and other high HIV prevalence settings.

7. Prevention of mother-to-child transmission

A Case Series of 104 Women Infected with HIV-1 via Blood Transfusion Postnatally: High Rate of HIV-1 Transmission to Infants through Breast-Feeding.


Liang and colleagues investigated transmission of human immunodeficiency virus type 1 (HIV-1) via breast-feeding by 104 Chinese mothers who acquired the infection through blood transfusion
postnatally. Of 106 children, 38 (35.8%) were infected. All children survived to age 5 years, and their survival curve was similar to that of their mothers. These findings suggest a high rate of HIV-1 transmission via breast-feeding when mothers were infected postnatally via blood transfusion, perhaps because of the higher viremia expected during the acute phase of infection. The course of disease among infected children was significantly less rapid than that among newborns infected perinatally, suggesting that a brief window of HIV-1-free life often enables the immune system of an infant to stave off rapid disease progression.

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Editors’ note: Although blood-selling practices were officially prohibited in China by 1995 and the Blood Transfusion Law was passed in 1998, some of the women in this cohort were infected by blood transfusions as late as 2000. This emphasises the importance of concrete local plans to reduce the time between the announcement of policies and their implementation. In this case study series of acutely infected, breastfeeding women, the HIV transmission rate of 35.8% was considerably higher than previous estimates of 9 to 16% for post-natal transmission through breast milk. The risk of HIV transmission rose significantly to 62.5% (95%CI, 35.4-84.9%) if mastitis or cracked nipples were reported. The low mortality rate of 13.2% in these children after a mean of 9.1 years in the absence of antiretroviral treatment suggests rapid evolution in the immune system capacity over the initial weeks and months of life leading to better viral control.

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Antiretroviral resistance after short-course regimens used to prevent mother-to-child transmission has consequences for later treatment. Directly comparing the prevalence of resistance after short-course regimens of highly active antiretroviral therapy and zidovudine plus single-dose nevirapine (ZDV/sdNVP) will provide critical information when assessing the relative merits of these antiretroviral interventions. In a clinical trial in Kenya, pregnant women were randomized to receive either ZDV/sdNVP or a short-course of highly active antiretroviral therapy through 6 months of breastfeeding. Plasma samples were collected 3-12 months after treatment cessation, and resistance to reverse transcriptase inhibitors was assessed using both a sequencing assay and highly sensitive allele-specific polymerase chain reaction assays. No mutations associated with resistance were detectable by sequencing in either the ZDV/sdNVP or highly active antiretroviral therapy arms at 3 months posttreatment, indicating that resistant viruses were not present in >20% of virus. Using allele-specific polymerase chain reaction assays for K103N and Y181C, the authors detected low levels of resistant virus in 75% of women treated with ZDV/sdNVP and only 18% of women treated with highly active antiretroviral therapy (P =0.007). Y181C was more prevalent than K103N at 3 months and showed little evidence of decay by 12 months. The study finding provides evidence that compared with ZDV/sdNVP, HAART reduces but does not eliminate nevirapine resistance.

Abstract only: 1

Editors’ note: This small Kenyan trial is the first study to compare directly the prevalence of HIV resistance after short-course antiretroviral treatment with standard prophylactic regimens. Of 58 women initially randomised, 40 women had plasma samples for analysis by sequencing assay and highly sensitive polymerase chain reaction. One study arm received zidovudine twice daily for 6 weeks before delivery, single-dose nevirapine during labour, and for the babies, single dose nevirapine. The women in the other study arm received twice-daily zidovudine, nevirapine, and 3TC for 6 weeks before and 6 months after delivery. The big difference seen in the levels of resistant virus 3 months or more after ceasing to take drugs may well be due to the fact that in the first arm, nevirapine was not accompanied by any other antiretroviral drug during labour. Antiretroviral treatment for 6 months did not eliminate nevirapine resistance, suggesting that after
nevirapine is stopped, treatment cessation strategies should include temporarily continuing zidovudine and 3TC to prevent single drug pressure caused by nevirapine’s longer half-life.

8. Structural interventions – sex work

HIV prevention while the bulldozers roll: Exploring the effect of the demolition of Goa’s red-light area.


Interventions targeting sex-workers are pivotal to HIV prevention in India. Community mobilisation is considered by the National AIDS Control Programme to be an integral component of this strategy. Nevertheless societal factors, and specifically policy and legislation around sex-work, are potential barriers to widespread collectivisation and empowerment of sex-workers. Between November 2003 and December 2005 Shahmanesh and colleagues conducted participatory observation and rapid ethnographic mapping with several hundred brief informant interviews, in addition to 34 semi-structured interviews with key-informants, 16 in-depth interviews with female sex-workers, and 3 focus-group-discussions with clients and mediators. This article provides a detailed examination of the demolition of Baina, one of India’s large red-light areas, in 2004, and one of the first accounts of the effect of dismantling the red-light area on the organisation of sex-work and sex-workers’ sexual risk. The results suggest that the concentrated and homogeneous brothel-based sex-work environment rapidly evolved into heterogeneous, clandestine and dispersed modes of operation. The social context of sex-work that emerged from the dust of the demolition was higher risk and less conducive to HIV prevention. The demolition acted as a negative structural intervention; a catastrophic event that fragmented sex-workers' collective identity and agency and rendered them voiceless and marginalised. The findings suggest that an abolitionist approach to sex-work and legislation or policy that either criminalises this large group of women, or renders them as invisible victims, will increase the stigma and exclusion they experience. For the targeted HIV prevention approaches advocated by the National AIDS Control Programme to be effective, there is a need for legislation and policy that supports sex-workers’ agency and self-organisation and enables them to create a safer working environment for themselves.

For Abstract click here: 1

Editors’ note: The authors of this thoughtful analysis were engaged in a study developing a participatory evidence-based HIV prevention intervention when the demolition of Baina started following a high court judgement. Because the dispersion and marginalisation of women following eviction would make the study impossible the researchers began documenting unfolding events and their effects on the community, as well as on the evolving relationship between the researchers and the community. This rich description helps understand how abolitionist discourses, whether religious or social reformist, converge to strip women who are sex workers of any agency, either by stigmatising them or by depicting them as victims by conflating sex work with trafficking. If you have wondered what a negative structural intervention is and does, and if you ever worked with communities, this is an article that you won’t be able to stop reading.
9. Treatment

When to start antiretroviral therapy in resource-limited settings.


The results of international clinical trials that are assessing when to initiate antiretroviral therapy will not be available for several years. The authors set out to inform HIV treatment decisions about the optimal CD4 threshold at which to initiate antiretroviral therapy in South Africa while awaiting the results of these trials by carrying out cost-effectiveness analysis of published data using a computer simulation model of HIV disease. The data were from randomized trials and observational cohorts in South Africa and the target population was HIV-infected patients in South Africa over a 5-year time horizon and over lifetime. The perspective was modified societal. The interventions considered were: no treatment, antiretroviral therapy initiated at a CD4 count less than 0.250 x 10^9 cells/L, and antiretroviral therapy initiated at a CD4 count less than 0.350 x 10^9 cells/L. The outcome measures were morbidity, mortality, life expectancy, medical costs, and cost-effectiveness. If 10% to 100% of HIV-infected patients are identified and linked to care, a CD4 count threshold for ART initiation of 0.350 x 10^9 cells/L would reduce severe opportunistic diseases by 22,000 to 221,000 and deaths by 25,000 to 253,000 during the next 5 years compared with ART initiation at 0.250 x 10^9 cells/L; cost increases would range from $142 million (10%) to $1.4 billion (100%). Either ART initiation strategy would increase long-term survival by at least 7.9 years, with a mean per-person life expectancy of 3.8 years with no ART and 12.5 years with an initiation threshold of 0.350 x 10^9 cells/L. Compared with an initiation threshold of 0.250 x 10^9 cells/L, a threshold of 0.350 x 10^9 cells/L has an incremental cost-effectiveness ratio of $1200 per year of life saved. Initiating antiretroviral therapy at a CD4 count less than 0.350 x 10^9 cells/L would remain cost-effective over the next 5 years even if the probability that the trial would demonstrate the superiority of earlier therapy is as low as 17%. This model does not consider the possible benefits of initiating antiretroviral therapy at a CD4 count greater than 0.350 x 10^9 cells/L or of reduced HIV transmission. Earlier initiation of antiretroviral therapy in South Africa will probably reduce morbidity and mortality, improve long-term survival, and be cost-effective. While awaiting trial results, treatment guidelines should be liberalized to allow initiation at CD4 counts less than 0.350 x 10^9 cells/L, earlier than is currently recommended.

For full text access click here: 1

Editors’ note: This cost-effectiveness analysis of 3 options (no treatment and treatment initiation thresholds of 250 and 350 CD4 cell counts) using a computer simulation to model HIV disease helps answer a critical question in the South African national context. What at the clinical outcomes and costs over the short-term (5 years) of different decisions on treatment initiation, taking into account the chance that the trials currently studying antiretroviral initiation will demonstrate a clinical benefit of antiretroviral treatment initiation at the 350 cell count level? Although randomised controlled trials, rather than models, are the gold standard for developing policy, models can help inform policy. Inadequate treatment capacity may exacerbate inequities in treatment access and this should be carefully monitored regardless of CD4 count entry criteria. Changes in the WHO treatment guidelines are likely to be announced in the coming months, provoking many countries which have not done so to consider how to strengthen their strategies for scale-up to universal access.

Effect of immunodeficiency, HIV viral load, and antiretroviral therapy on the risk of individual malignancies (FHDH-ANRS CO4): a prospective cohort study.

The relative roles of immunodeficiency, HIV viral load, and combination antiretroviral therapy in the onset of individual cancers have rarely been examined. The authors examined the effect of these factors on the risk of specific cancers in patients infected with HIV-1. They investigated the incidence of both AIDS-defining cancers (Kaposi's sarcoma, non-Hodgkin lymphoma, and cervical cancer) and non-AIDS-defining cancers (Hodgkin's lymphoma, lung cancer, liver cancer, and anal cancer) in 52,278 patients followed up in the French Hospital Database on HIV cohort during 1998-2006 (median follow-up 4.9 years, IQR 2.1-7.9; 255,353 person-years). They tested 78 models with different classifications of immunodeficiency, viral load, and combination antiretroviral therapy with Poisson regression. Current CD4 cell count was the most predictive risk factor for all malignancies apart from anal cancer. Compared with patients with CD4 count greater than 500 cells per μL, rate ratios ranged from 1.9 (95% CI 1.3-2.7) for CD4 counts 350-499 cells per μL to 25.2 (17.1-37.0) for counts less than 50 cells per μL for Kaposi's sarcoma (p<0.0001), from 1.3 (0.9-2.0) to 14.8 (9.7-22.6) for non-Hodgkin lymphoma (p<0.0001), from 1.2 (0.7-2.2) to 5.4 (2.4-12.1) for Hodgkin's lymphoma (p<0.0001), from 2.2 (1.3-3.6) to 8.5 (4.3-16.7) for lung cancer (p<0.0001), and from 2.0 (0.9-4.5) to 7.6 (2.7-20.8) for liver cancer (p<0.0001). For cervical cancer, they noted a strong effect of current CD4 (rate ratios 0.7 per log(2), 95% CI 0.6-0.8; p=0.0002). The risk of Kaposi's sarcoma and non-Hodgkin lymphoma increased for current plasma HIV RNA greater than 100,000 copies per mL compared with patients with controlled viral load (RR 3.1, 95% CI 2.3-4.2, p<0.0001; and 2.9, 2.1-3.9, p<0.0001, respectively), whereas combination antiretroviral therapy was independently associated with a decreased incidence (0.3, 0.2-0.4, p<0.0001; and 0.8, 0.6-1.0, p=0.07, respectively). The rate ratios of cervical cancer for those receiving combination antiretroviral therapy was 0.5 (0.3-0.9; p=0.03). The risk of anal cancer increased with the time during which the CD4 count was less than 200 cells per μL (1.3 per year, 1.2-1.5; p=0.0001), and viral load was greater than 100,000 copies per mL (1.2 per year, 1.1-1.4, p=0.005). Combination antiretroviral therapy would be most beneficial if it restores or maintains CD4 count above 500 cells per μL, thereby indicating an earlier diagnosis of HIV infection and an earlier treatment initiation. Cancer-specific screening programmes need to be assessed in patients with HIV.

For Abstract click here: 1

Editors’ note: Patients with HIV have a higher risk than does the general population of both AIDS-defining and non-AIDS-defining cancers. However, since the introduction of antiretroviral treatment, the incidence of AIDS-defining cancers has decreased, whereas that of non-AIDS-defining cancers has increased. Both the size of this French cohort and its length of follow-up allowed investigation of seven specific cancers, finding that the risk of all of them increased with immunodeficiency. Among patients with Kaposi’s sarcoma, men who have sex with men are over-represented. Among patients with liver cancer and lung cancer, injecting drug users are over-represented. Antiretroviral treatment to keep CD4 counts above 500 cells combined with regular cervical-screening programmes for all HIV-positive women and early detection of anal cancer in men could help improve HIV-related cancer outcomes.

10. Basic Science

Multiple-infection and recombination in HIV-1 within a longitudinal cohort of women.


Recombination between strains of HIV-1 only occurs in individuals with multiple infections, and the incidence of recombinant forms implies that multiple infection is common. Most direct studies indicate that multiple infection is rare. Templeton and colleagues set out to determine the rate of multiple infection in a longitudinal study of 58 HIV-1 positive participants from The Women’s Interagency HIV Study with a richer sampling design than previous direct studies, and they
investigated the role of recombination and sampling design on estimating the multiple infection rate. 40% of their sample had multiple HIV-1 infections. This rate of multiple infection is statistically consistent with previous studies once differences in sampling design are taken into account. Injection drug use significantly increased the incidence of multiple infections. In general there was rapid elimination of secondary strains to undetectable levels, but in 3 cases a superinfecting strain displaced the initial infecting strain and in two cases the strains coexisted throughout the study. All but one secondary strain was detected as an inter- and/or intra-genic recombinant. Injection drug use significantly increased the rate of observed recombinants. The study’s multiple infection rate is consistent with rates estimated from the frequency of recombinant forms of HIV-1. The fact that the results are also consistent with previous direct studies that had reported a much lower rate illustrates the critical role of sampling design in estimating this rate. Multiple infection and recombination significantly add to the genetic diversity of HIV-1 and its evolutionary potential, and injection drug use significantly increases both.

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Editors’ note: Multiple infection may mean co-infection, where the host is infected by two or more strains of HIV, or superinfection, where the initial infection is followed by a later secondary infection. In this detailed genetic study of 23 women with multiple infections, 10 were detected as potentially co-infected at the first study visit and 13 were definitely superinfected during the study. All of them experienced recombination between pol and env genes, with most eventually losing the recombinant strain. Among the 13 superinfected women, the original strain was replaced by the second strain in 3 cases. This suggests that most of the time selection works to eliminate recombinants and superinfecting strains unless they have very superior fitness and competitive ability. However, the bottom line is that initial HIV infection does not protect against superinfection, underscoring the personal benefits of positive prevention for people living with HIV.

Editors’ note: This excellent review is a must-read for anyone wanting to learn in a nutshell what is known about the effects of malnutrition on HIV disease progression, the causes of increased mortality in malnourished people on antiretroviral treatment, and the advantages and
disadvantages of the macronutrient supplements that are readily available now in low- and middle-income countries. The target intake should be 2100 kcal/day for adults increased by a additional 30% of patients with advanced HIV infection. Among the questions for future trials to address are the proportion of daily calories to supply, choice of supplement, duration of supplementation, acceptability and behaviour, logistics, and programme exit criteria.

Deworming helminth co-infected individuals for delaying HIV disease progression.

The HIV-1 pandemic has disproportionately affected individuals in resource-constrained settings where other infectious diseases, such as helminth infections, also are highly prevalent. There are biologically plausible reasons for possible effects of helminth infection in HIV-1-infected individuals, and findings from multiple studies suggest that helminth infection may adversely affect HIV-1 progression. Since initial publication of this review (Walson 2007), additional data from randomized controlled trials has become available. Walson and colleagues therefore sought to evaluate all currently available evidence to determine if treatment of helminth infection in HIV-1 co-infected individuals impacts HIV-1 progression. They set out to determine if treating helminth infection in individuals with HIV-1 can reduce the progression of HIV-1 as determined by changes in CD4 count, viral load, or clinical disease progression. In this 2008 update, the authors searched online for published and unpublished studies in The Cochrane Library, MEDLINE, EMBASE, CENTRAL, and AIDSEARCH. They also searched databases listing conference abstracts, scanned reference lists of articles, and contacted authors of included studies. The authors searched for randomized controlled trials and quasi-randomized controlled trials that compared HIV-1 progression as measured by changes in CD4 count, viral load, or clinical disease progression in HIV-1 infected individuals receiving anti-helminthic therapy. Data regarding changes in CD4 count, HIV-1 RNA levels, and/or clinical staging after treatment of helminth co-infection were extracted from identified studies. Of 7,019 abstracts identified (6,384 from original searches plus 635 from updated searches), 17 abstracts were identified as meeting criteria for potential inclusion (15 from previous review plus an additional two randomized controlled trials). After restricting inclusion to randomized controlled trials, a total of three studies were eligible for inclusion in this updated review. All three trials showed individual beneficial effects of helminth eradication on markers of HIV-1 disease progression (HIV-1 RNA and/or CD4 counts). When data from these trials were pooled, the analysis demonstrated significant benefit of deworming on both plasma HIV-1 RNA and CD4 counts. To date, three randomized controlled trials have evaluated the effects of deworming on markers of HIV-1 disease progression in helminth and HIV-1 co-infected individuals. All trials demonstrate benefit in attenuating or reducing plasma viral load and/or increasing CD4 counts. When taken together, there is evidence of benefit for deworming HIV-1 co-infected adults. Given that these studies evaluated different helminth species and different interventions, further trials are warranted to evaluate species-specific effects and to document long-term clinical outcomes following deworming.

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Editors’ note: Between one-third and one-half of the global population is infected with at least one species of helminth (worms), with most infections found in low- and middle-income countries. Three randomised, controlled trials have now shown the short-term benefit on markers of HIV disease progression (CD4 counts, viral load) of treating helminth infection. These short term trials evaluated different interventions and different helminth infections (schistosomiasis, soil-transmitted helminths, and lymphatic filariasis) so it is premature to recommend empiric anti-helminthic therapy or routine helminth screening of HIV-infected adults. What is needed now are larger trials with longer follow-up to determine whether there are significant meaningful differences in clinical progression. In the meantime, helminth infection should be treated when it is found.
12. Young people

Early Coital Debut and Associated HIV Risk Factors Among Young Women and Men in South Africa.


Young people in South Africa are at high risk of HIV infection. Because first sexual experiences may influence a young person’s HIV risk, a better understanding of coital debut is needed. Data from a nationally representative survey that included 7,692 sexually active South African youth aged 15-24 were used to assess characteristics related to sexual debut and to respondents’ first sexual partner. Poisson regression analyses were conducted to identify relationships among these characteristics and partner age differences, early coital debut (i.e., before age 15), forced sex with one’s first partner and nonuse of condoms at first sex. Eighteen percent of young men and 8% of young women reported early coital debut. The likelihood of early debut was elevated among females and males who had had an older first partner (adjusted prevalence ratio, 1.1 per year) and among females who had had forced sex (2.5). Lack of condom use at first sex was associated with early coital debut (1.5) and forced sex (1.6) for males. Among females, the likelihood of nonuse was elevated for respondents who had had an early debut but had not had forced sex (1.3), and among those who had had both a later debut and forced sex (1.4). Early coital debut is associated with factors that may increase a young person’s risk for HIV infection, such as forced sex and having older partners. Intervention efforts should encourage youth to delay coital debut and promote strategies to make young people’s first sexual experience safer.

For full text access click here: 1

Editors’ note: The majority of young people in this nationally representative survey did not report early coital debut and comparison with previous studies in the same age-group in South Africa suggests that age at sexual debut has not changed significantly during the past decade. Because HIV prevalence is so high in South Africa, young people should be encouraged to delay the onset of first penetrative sex. Concerted efforts are required to address the contractual and structural factors that can make young people’s first sexual experiences safer in high HIV prevalence contexts.
That was *HIV this week*, signing off.

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**Editors’ notes on journal access**

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