Welcome to the 90th issue of *HIV This Week*! In this issue, we cover the following topics:

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Don’t forget that you can always find a wealth of information on the HIV epidemic and responses to it at www.unaids.org.
1. Civil Society Responses

The effects of national and international HIV/AIDS funding and governance mechanisms on the development of civil-society responses to HIV/AIDS in East and Southern Africa

Kelly KJ, Birdsall K. AIDS Care. 2010;22 Suppl 2:1580-7

This study takes stock of the exponential growth in the number of new civil-society organisations working in the HIV field in East and Southern Africa during the period 1996-2004. Kelly and Birdsall researched this development through a survey of 439 civil-society organisations in six countries and case studies focused on the evolution of community responses to HIV in specific communities in eight countries. The authors describe the types of civil-society organisations that emerged, their relationships with governments and donors, and their activities, organisational characteristics, and funding requirements. The data presented show that the vision of social mobilisation of HIV responses through community-level organisations has faced strong external challenges. Evidence from survey data, national HIV spending assessments, and case studies shows that in some respects the changing international aid environment undermines the prospects for development of the civil-society sector’s contributions in HIV responses. Of particular interest is to understand how the “Three Ones” and the Paris Declaration on Aid Effectiveness have reshaped international funding for HIV responses. There has been relatively little attention paid to the impact of the new management and funding modalities - including national performance frameworks, general budget support, joint funding arrangements, and basket funds - on civil-society agencies at the forefront of community HIV responses. Evidence is presented to show that in important respects the new modalities limit the unique contribution that civil-society organisations can make to national HIV responses. It is also shown that the drive to rapidly intensify the scale of HIV responses has involved using community organisations as service providers for externally formulated programmes. The authors discuss this as a strong threat to the development of sustainable civil-society economies as well as to civil-society organisations’ diversity and responsiveness. The ways in which civil-society organisations are responding to these challenges are discussed, pointing to possibilities for a new phase of development of the civil-society sector.


Editors’ note: If you work at country level, or support those that do; if you are interested in capacity building; or if you want to know how AIDS financing, the Three Ones, and the Paris Declaration on Aid Effectiveness have affected civil society responses to HIV, then this is essential reading for you. Surveys in high HIV prevalence countries (Lesotho, Malawi, Mozambique, Namibia, Swaziland, and Zambia) and case studies in these 6 countries plus South Africa and Tanzania reveal the concerning effects that AIDS funding architecture has had on the work of community- and national-level civil society organisations. A ‘scaling out’ has occurred of medium-sized national non-governmental organisations with long, strong track records that had previously received financial and capacity-building support through direct funding from bilateral donors. Pioneering, ‘on the ground’ civil society organisations, often the heart of the community-driven response reaching those most in need, now have fragile futures due to the unpredictability of funding. Further, that funding does not include investment in basic operating costs, organisational planning, or capacity development. National-level and community-level civil society organisations act predominantly now in service-provision roles, often as sub-contractors without opportunities to develop capacity to design, plan, budget, or implement programmes that are not externally mandated. Clearly, there is a need for long-term strategic thinking at national and international levels about how best to strengthen civil society’s country- and community-level contribution to the response – it is losing its diversity and its voice.
2. Condoms

Exploring the condom gap: is supply or demand the limiting factor? – Condom access and use in an urban and a rural setting in Kilifi district, Kenya


The objective of this study was to explore the extent of the condom gap, investigating the relative roles of supply-side and demand-side factors in determining condom use through GPS mapping of condom outlets, and a population-based survey. An urban and a rural site were selected within the Epidemiological and Demographic Surveillance Site in Kilifi district, Kenya. Potential condom outlets (n = 281) were mapped and surveyed, and questionnaires on condom access and use (n = 630) were administered to a random sample of men and women aged 15-49. Multivariate logistic regression was performed to assess the relative roles of supply-side and demand-side barriers on condom use. The median straight-line distance to free condoms was 18-fold higher in the rural versus the urban site. Among sexually active respondents, 42% had ever used a condom, and 23% had used a condom over the past 12 months, with lower levels among rural versus urban respondents (P < 0.05). The mean number of condoms used was 2.2/person per year among all sexually active individuals (condom users and nonusers), amounting to 8.2% protected sex acts/person per year. The adjusted odds of condom use (past 12 months) were 8.1 times greater among individuals experiencing no supply-side or demand-side barriers, compared with individuals experiencing both types of barriers. Despite low levels of usage and the presence of supply-side and demand-side barriers, reported unmet need for condoms was low. There is an urgent need for renewed condom promotion efforts aimed at building demand, in addition to improving physical access, in resource-limited settings with generalized HIV epidemics in sub-Saharan Africa.


Editors’ note: If HIV prevalence where you lived was 5%, how far would you walk to buy a condom (0.15 USD for a 3-pack)? How far would you walk for a free condom? Two-thirds of the people in this study were living on less than a dollar a day so you might think cost would be the major deterrent to accessing and using condoms. The picture is more complex. There were gaps in the physical availability of condoms – the shortest route to the nearest free condom outlet for rural respondents was almost 5 kilometres and less than 1 % of all condom outlets (none rural) had female condoms. But the biggest barriers to condom use were on the demand side: 81% of people had one or more demand side barriers whereas 30% had supply side barriers. People with neither were 8 times more likely to have used condoms in the previous 12 months. The most striking finding of this study regards unmet need: only 7% of people reported having ever wanted to access or use a condom and been unable to do so. There is an imperative here, as in many parts for the world, to increase demand and perceived need for condoms. After all, condoms remain the single, most efficient available technology to reduce sexual transmission of HIV—6000 adults become infected daily, the majority through unprotected sex.

3. HIV and maternal mortality

Strengthening HIV services for pregnant women: an opportunity to reduce maternal mortality rates in Southern Africa/sub-Saharan Africa


Reliable data from South Africa emanating from WHO recommendations for the Safe Motherhood programme underscore HIV-related illness as the most common cause of maternal deaths. The strengthening of HIV services for pregnant women, especially in countries with a high burden of HIV infection, will reduce HIV-related and un-related maternal mortality rates. High-quality and complete data on maternal deaths is a critical foundation for reliably monitoring temporal trends in maternal deaths, and causes thereof, but needs substantial strengthening in many resource-constrained settings.
HIV is an increasing contributor to direct and indirect causes of maternal deaths in sub-Saharan Africa. A review of published data on maternal deaths and its association with HIV shows that reliable data come from the Confidential Enquiries into Maternal Deaths from South Africa, population-based surveys in sentinel populations, and facility-based data. Despite an increase in knowledge of the HIV status of pregnant women and the initiation of antiretroviral treatment, reversals in trends towards increased maternal deaths are not being observed. The strengthening of HIV services provides an opportunity to alter HIV epidemic trajectories and reduce maternal deaths.


Editors’ note: The figures are stark: each year 80 million women have unwanted pregnancies and a third of maternal deaths could be prevented through the promotion and uptake of family planning. Each year there are more than 2 million pregnancies in women living with HIV and, in resource-constrained settings, HIV accounts for an estimated ten-fold increased risk of maternal death. This is not because pregnancy increases HIV disease progression—it does not do so in asymptomatic women—but rather because symptomatic women with HIV infection are at greater risk of dying from infectious diseases. Maternal mortality is defined as a death during pregnancy or within 42 days of the end of pregnancy from any cause related to or aggravated by pregnancy or its management, not including accidental or incidental causes. Maternal deaths are underestimated because not all women use health care facilities during pregnancy, for delivery, or for post-pregnancy care – and facility-based reports are the prime source of maternal mortality data. The action agenda is clear. To get Millennium Development Goal 5 on track by reducing the contribution of AIDS to maternal mortality, we must prevent HIV infection in women and girls, prevent unwanted pregnancies, expand HIV testing and counselling, accelerate initiation of antiretroviral treatment in pregnant women who are HIV-positive, and strengthen service delivery and integration of HIV care and obstetric services, along with data collection to track progress.

4. Host genetics

Host genetics and HIV-1: the final phase?


This is a crucial transition time for human genetics in general, and for HIV host genetics in particular. After years of equivocal results from candidate gene analyses, several genome-wide association studies have been published that looked at plasma viral load or disease progression. Results from other studies that used various large-scale approaches - small interfering RNA (siRNA) screens, transcriptome or proteome analysis, comparative genomics - have also shed new light on retroviral pathogenesis. However, most of the inter-individual variability in response to HIV-1 infection remains to be explained: genome resequencing and systems biology approaches are now required to progress toward a better understanding of the complex interactions between HIV-1 and its human host.


Editors’ note: Highly exposed, yet uninfected, people such as the 5% of men with severe haemophilia born before 1979 who did not become infected, the cohorts of men who have sex with men reporting high exposure levels, and the famous Nairobi sex workers have exceptional resistance to HIV infection. Analysing their genetic make-up improves our understanding of genetic influences on susceptibility, as will comparing the genetic make-up of people with HIV infection with that of uninfected controls. So far, most genetic studies have focused on people with Western European ancestry with the result that we lack information on genetic diversity. Thus far, we have only found variation in CCR5 to be a significant human genetic determinant of HIV acquisition while human leukocyte antigen (HLA) class is the most prominent genetic determinant of differences in viral load set point and CD4 count decline. Because some clinically stable people who become superinfected have very rapid disease progression and because marked
differences have been documented in viral load set point between donor and recipients in HIV transmission pairs, the virus itself must be important too. Understanding individual host-virus interaction differences is key to both developing HIV vaccines and anticipating how people living with HIV will respond to treatment. The HIV host genetic research field is using genome analysis and systems biology high throughput quantitative modelling techniques to describe human genetic influences on HIV. This review is an interesting read.

5. HIV Prevention trials

Apples and oranges? Interpreting success in HIV prevention trials

In the last decade, several large-scale clinical trials evaluating the efficacy of novel HIV prevention products have been completed, and eight are currently underway or about to be reported. Little attention has been given in the literature to the level of protection sufficient to warrant introduction, and there is concern that using the term "efficacy" to describe the effect of user-controlled methods such as microbicides may mislead policymakers. The authors reviewed how the fields of family planning, vaccine science, and mathematical modelling understand and use the terms efficacy and effectiveness, and explore with simple mathematical models how trial results of user-controlled products relate to common understandings of these terms. Each field brings different assumptions, a different evidence base, and different expectations to interpretations of efficacy and effectiveness - a reality that could cloud informed assessment of emerging data. When making judgments on the utility of new health technologies, it is important to use standards that yield appropriate comparisons for the innovation and that take into account the local epidemic and available alternatives.


Editors’ note: Deciding how good is good enough for a new HIV prevention technology to be worth introducing in your setting depends on a number of factors, including the risk of HIV infection—but it also depends on how randomised controlled trial findings are understood and whether a method is user-controlled or provider-controlled. The term ‘efficacy’ is used most frequently in reporting vaccine trial results where it measures the biological effect of a vaccine since there is objective evidence of whether a vaccine dose has been administered or not. Similarly, male circumcision, a one-time surgical procedure, is considered after three trials to be 50-60% efficacious in reducing HIV risk in heterosexual men. The term ‘efficacy’ has been used recently referring to the protection against HIV seen in the iPrEx chemoprevention trial among men who have sex with men who were in the active arm of the study and had detectable drug levels. To further complicate matters, trials measure protection achieved over time while modellers use ‘per-sex-act efficacy’ in modelling the potential impact of introducing a new prevention modality. However, most HIV prevention trial results report effectiveness, a combined measure of the biological efficacy of a product and its pattern of use in the trial. With respect to recently reported oral and topical pre-exposure prophylaxis trial results, it is evident that designing effective strategies to improve pill-taking behaviour or gel use, in addition to correct and consistent use of condoms, will be a key consideration, along with cost, demand, viral resistance, acceptability, incremental benefits, etc. in influencing policy makers decisions to add chemoprevention to their programming.

6. Discordant couples

HIV-1 transmission among HIV-1 discordant couples before and after the introduction of antiretroviral therapy in Rakai, Uganda
To evaluate the impact of antiretroviral therapy on HIV-1 transmission rates among HIV-1 discordant couples in Rakai, Uganda, Reynolds and colleagues studied HIV-1 discordant couples which were retrospectively identified between 2004 and 2009. Study participants underwent annual screening for HIV-1 and were interviewed to evaluate risk behaviours. Participants were offered voluntary counselling and testing and provided with risk reduction counselling. Free antiretroviral therapy was offered to participants with a CD4 cell count ≤250 cells/ml or WHO stage IV disease. HIV-1 incidence and sexual risk behaviours were compared before and after the HIV-1 positive index partners started antiretroviral therapy. Two hundred and fifty HIV-1 discordant couples were followed between 2004-2009 and 32 HIV-1 positive partners initiated antiretroviral therapy. Forty two HIV-1 transmissions occurred over 459.4 person-years prior to antiretroviral therapy initiation, incidence 9.2/100 person years, (95% CI 6.59, 12.36). In the 32 couples in which the HIV-1 index partners started antiretroviral therapy, no HIV-1 transmissions occurred during 53.6 person-years. The 95% confidence interval (CI) for the incidence rate difference was (-11.91, -6.38, p = 0.0097). Couples reported more consistent condom use during antiretroviral therapy use but there was no significant difference in the number of sexual partners or other risk behaviours. Viral load was markedly reduced in persons on antiretroviral therapy. HIV-1 transmission may be reduced among HIV-1 discordant couples after initiation of antiretroviral therapy due to reductions in HIV-1 viral load and increased consistent condom use.

Editors' note: This observational study of 250 HIV-serodiscordant couples (58% had a male index positive partner) documented no HIV transmission in the 32 couples in which antiretroviral therapy was started at CD4 cell counts under 250. In comparison, the HIV transmission rate in couples where treatment had not yet been initiated was 9.2 per 100 person years. The sample size is small and condom use may have confounded the findings making it unclear how much antiretroviral treatment contributed to the reduction in HIV transmission. Consistent condom use increased significantly in those starting treatment, rising from 14.3% to 53.7% with any partner. Nonetheless, the findings provide support for the hypothesis being tested in the HPTN 052 trial that antiretroviral treatment can prevent HIV transmission in HIV-discordant couples.

Pregnancy and HIV transmission among HIV-discordant couples in a clinical trial in Kisumu, Kenya


A large proportion of new HIV infections in sub-Saharan Africa occur in stable HIV-discordant partnerships. In some couples, the strong desire to conceive a child may lead to risky behaviour despite knowledge of discordant serostatus. Brubaker and colleagues’ objective was to compare HIV transmission between discordant couples who did and did not conceive during participation in a clinical trial. Five hundred and thirty-two HIV-discordant couples were followed for up to 2 years in Kisumu, Kenya as part of the Partners in Prevention HSV/HIV Transmission Study. Quarterly HIV-1 antibody and urine pregnancy test results were analysed. Forty-one HIV-1 seroconversions occurred over 888 person-years of follow-up, resulting in an annual incidence of 4.6/100 person-years. Twenty seroconversions occurred among 186 HIV-1-uninfected individuals in partnerships in which pregnancy occurred (10.8% of HIV-1-negative partners in this group seroconverted), in comparison to 21 seroconversions among 353 uninfected individuals in partnerships in which pregnancy did not occur (5.9% of HIV-1-negative partners seroconverted), resulting in a relative risk of 1.8 [95% confidence interval 1.01-3.26; P<0.05]. Pregnancy was associated with an increased risk of HIV seroconversion in discordant couples. These data suggest that the intention to conceive among HIV discordant couples may be contributing to the epidemic.

Editors' note: This study did not collect information about intention to conceive so it is actually not possible to know whether the pregnancies that occurred are a marker of unprotected intercourse rather than intention to conceive. Women enrolled in this study had verbally agreed to delay pregnancy until the end of the trial and were provided access to condoms and hormonal contraception free of charge. Despite this, 35% of them became pregnant, with no significant difference in the pregnancy rate between those who had HIV infection and those who did not. In the 20 couples in which both pregnancy and HIV seroconversion occurred, 12 women and 8 men became infected. Why HIV transmission was more likely to occur in couples who became pregnant is unclear. No genetic fingerprinting is reported to allow linkage between the index person's virus and that of the couple member who seroconverted. If the transmissions are all linked, does pregnancy somehow increase susceptibility or transmissibility? In any case, this study underscores the importance of a harm reduction approach to counselling about reproductive choice which includes counselling about timed unprotected intercourse, home insemination, or confirmation of viral suppression.

7. Treatment outcomes

Adjusting mortality for loss to follow-up: analysis of five ART programmes in sub-Saharan Africa


Evaluation of antiretroviral treatment antiretroviral therapy programmes in sub-Saharan Africa is difficult because many patients are lost to follow-up. Outcomes in these patients are generally unknown but studies tracing patients have shown mortality to be high. The authors adjusted programme-level mortality in the first year of antiretroviral treatment antiretroviral therapy for excess mortality in patients lost to follow-up. Treatment-naïve patients starting combination antiretroviral therapy in five programmes in Côte d'Ivoire, Kenya, Malawi, and South Africa were eligible. Patients whose last visit was at least nine months before the closure of the database were considered lost to follow-up. The authors filled missing survival times in these patients by multiple imputation, using estimates of mortality from studies that traced patients lost to follow-up. Data were analyzed using Weibull models, adjusting for age, sex, antiretroviral therapy regimen, CD4 cell count, clinical stage, and treatment programme. A total of 15,915 HIV-infected patients (median CD4 cell count 110 cells/µL, median age 35 years, 68% female) were included; 1,001 (6.3%) were known to have died and 1,285 (14.3%) were lost to follow-up in the first year of antiretroviral therapy. Crude estimates of mortality at one year ranged from 5.7% (95% CI 4.9-6.5%) to 10.9% (9.6-12.4%) across the five programmes. Estimated mortality hazard ratios comparing patients lost to follow-up with those remaining in care ranged from 6 to 23. Adjusted estimates based on these hazard ratios ranged from 27% to 73% across programmes. Naïve survival analysis ignoring excess mortality in patients lost to follow-up may greatly underestimate overall mortality, and bias antiretroviral therapy programme evaluations. Adjusted mortality estimates can be obtained based on excess mortality rates in patients lost to follow-up.


Editors' note: Loss to follow-up may occur because a patient has died, transport and other costs are too high to continue treatment, HIV-related stigma may have intervened, or treatment adherence has been compromised for other reasons. This research does not focus on how to address loss to follow-up programmatically but rather on how best to adjust antiretroviral programme mortality rates for loss to follow-up. Mortality is the most definitive outcome in life and programmes must strive to measure it correctly and reduce it. The basic question is how much loss to follow-up is due to death. Treating loss to follow-up as a missing data problem, these researchers obtained adjusted mortality estimates used modelling techniques to impute survival times based on plausible estimates from studies that traced individuals lost to follow-up. They report first year adjusted mortality ranging from 10 to 17%. Programmes should adjust their mortality
statistics to account for likely rates of mortality among patients lost to follow-up and focus on starting treatment earlier and diagnosing opportunistic infections and cancers in order to bring those mortality rates down.

8. Gender

No association between HIV and intimate partner violence among women in 10 developing countries


Intimate partner violence has been reported to be a determinant of women's risk for HIV. The authors examined the relationship between women's self-reported experiences of intimate partner violence in their most recent relationship and their laboratory-confirmed HIV serostatus in ten low- to middle-income countries. Data for the study came from the most recent Demographic and Health Surveys conducted in Dominican Republic, Haiti, India, Kenya, Liberia, Malawi, Mali, Rwanda, Zambia and Zimbabwe. Each survey population was a cross-sectional sample of women aged 15-49 years. Information on intimate partner violence was obtained by a face-to-face interview with the mother with an 81.1% response rate; information on HIV serostatus was obtained from blood samples with an 85.3% response rate. Demographic and socioeconomic variables were considered as potentially confounding covariates. Logistic regression models accounting for multi-stage survey design were estimated individually for each country and as a pooled total with country fixed effects (n=60,114). Country-specific adjusted odds ratios for physical or sexual intimate partner violence compared to neither ranged from 0.45 [95% confidence interval (CI): 0.23-0.90] in Haiti to 1.35 [95% CI: 0.95-1.90] in India; the pooled association was 1.03 [95% CI: 0.94-1.13]. Country-specific adjusted odds ratios for physical and sexual intimate partner violence compared to no sexual intimate partner violence ranged from 0.41 [95% CI: 0.12-1.36] in Haiti to 1.41 [95% CI: 0.26-7.77] in Mali; the pooled association was 1.05 [95% CI: 0.90-1.22]. Intimate partner violence and HIV were not found to be consistently associated amongst ever-married women in national population samples in these lower income countries, suggesting that intimate partner violence is not consistently associated with HIV prevalence worldwide. More research is needed to understand the circumstances in which intimate partner violence and HIV are and are not associated with one another.


Editors’ note: These ten countries were chosen from more than 80 countries because only their Demographic and Health Surveys (DHS) included HIV testing and a domestic violence module. Of 140,837 women offered HIV testing and 145,042 women offered the domestic violence module, 60,795 women provided dried blood spot samples for HIV testing and answered questions about their experiences of intimate partner violence. They had to be married or have been married so this analysis is of ever-married women only. Indian women comprised 49.4% of the study. The results show important country variations with HIV prevalence ranging from 24.1% in Zimbabwe to 0.5% in India. Almost a third of women (32%) reported having experienced some form of intimate partner violence in their most recent sexual relationship. Although unadjusted analyses found intimate partner violence to be associated with a small, significant increase in HIV prevalence, this relationship weakened once demographic and social factors were accounted for. Further, this cross-sectional dataset allowed no conclusion about causal association as it is impossible to determine which came first, the violence or HIV infection. Nonetheless, observational studies have found intimate partner violence to be associated with increased HIV risk in southern and eastern Africa and India and interventions to empower women in South Africa have reduced risk behaviours for HIV acquisition. In any case, intimate partner violence is a violation of human rights with many negative consequences which should be addressed in its own right through broad public health coalitions.
9. Basic Science

Origin and evolution of HIV-1 in breast milk determined by single genome amplification and sequencing


HIV transmission via breastfeeding accounts for a considerable proportion of infant HIV acquisition. However, the origin and evolution of the virus population in breast milk, the likely reservoir of transmitted virus variants, are not well-characterized. In this study, HIV envelope (env) genes were sequenced from virus variants amplified by single genome amplification from plasma and milk of twelve chronically HIV-infected, lactating Malawian women. Maximum-likelihood trees and statistical tests of compartmentalization revealed interspersion of plasma and milk HIV env sequences in the majority of subjects, indicating limited or no compartmentalization of milk virus variants. However, phylogenetic tree analysis further revealed monotypic virus variants that were significantly more frequent in milk (median proportion of identical viruses: 29.5%, range: 0-61%) than plasma (median proportion of identical viruses: 0%, range: 0-26%) (p = 0.002), suggesting local virus replication in the breast milk compartment. Moreover, clonally-amplified virus env genes in milk produced functional virus envs that were all CCR5-tropic. Milk and plasma virus envs had similar predicted phenotypes and neutralization sensitivity to broadly neutralizing antibodies in both transmitting and nontransmitting mothers. Finally, phylogenetic comparison of longitudinal milk and plasma virus env sequences revealed convergent virus evolution and new clonal amplification of evolved virus env genes in milk. The limited compartmentalization and clonal amplification of evolving, functional viruses in milk indicates continual seeding of the mammary gland by blood virus variants, followed by transient local replication of these variants in the breast milk compartment.


Editors’ note: Viral load in breast milk is correlated with risk of HIV transmission through breastfeeding. This mode of transmission may account for nearly half of new infant infections in resource-constrained settings in which antiretroviral prophylaxis or antiretroviral treatment during breastfeeding or safe formula feeding are not available. This study found no evidence of viral evolution in the breast which contrasts with the differences seen between plasma virus variants and genital tract variants. This lack of what is called phylogenetic compartmentalisation in breast milk is encouraging but the finding of local production of virus means that efforts to reduce viral load in milk cannot rely solely on bringing down plasma viral load. Immunologic and antiretroviral drug interventions to reduce breast milk virus load will need to target trafficking of virus into the breast which seeds the mammary gland, as well as local replication of virus by productively infected cells.

Biomarkers of immune dysfunction in HIV


HIV infection is characterized by chronic immune system activation and inflammatory cytokine production. This review highlights recent developments using plasma and cellular biomarkers of immune system activation and dysfunction to predict mortality and opportunistic disease in HIV-infected individuals. HIV infection results in features characteristic of early aging of the immune system or 'immune senescence', driven by chronic antigen exposure and immune system activation. Microbial translocation of gut bacterial components is associated with chronic immune activation and possibly systemic inflammation. Antiretroviral therapy may not fully normalize this condition. Baseline elevations of certain biomarkers of inflammation or coagulopathy, notably interleukin-6, C-reactive protein, and D-dimer, have been associated with mortality or opportunistic disease, after adjustment for appropriate variables, in several large
randomized clinical trials. It is not known if elevated interleukin-6 or C-reactive protein causes this morbidity and mortality or if they are simply surrogate markers of a global inflammatory state. Several inflammatory biomarkers appear to add to our ability to predict mortality or opportunistic disease in HIV-infected individuals. Before biomarkers will be useful, it will be necessary to identify interventions that moderate biomarker levels, and then determine if this moderation attenuates disease outcomes.


Editors’ note: There are some striking similarities between biomarker changes seen in the immune system during the aging process and those seen in HIV infection. In fact, the ongoing inflammation associated with aging is described as ‘inflamm-aging’. Inflammation plays a role in cancer, cardiovascular disease, metabolic, bone, kidney, and liver disease in the general population so it is not surprising that people living with HIV who have chronic immune system activation are more at risk of these diseases. This review is an excellent summary of the state of our knowledge on the role of each biomarker: plasma or serum biomarkers as well as cellular markers of immune dysfunction. Antiretroviral therapy does reduce one biomarker, D-dimer, and the START (Strategic Timing of Antiretroviral Therapy) study may help validate the concept of ‘biomarker-guided’ antiretroviral therapy.

10. National responses

Decision making for HIV prevention and treatment scale up: bridging the gap between theory and practice

Alistar SS, Brandeau ML. Med Decis Making. 2010 Dec 29

Effectively controlling the HIV epidemic will require efficient use of limited resources. Despite ambitious global goals for HIV prevention and treatment scale up, few comprehensive practical tools exist to inform such decisions. Alistar and colleagues briefly summarize modelling approaches for resource allocation for epidemic control, and discuss the practical limitations of these models. They describe typical challenges of HIV resource allocation in practice and some of the tools used by decision makers. The authors identify the characteristics needed in a model that can effectively support planners in decision making about HIV prevention and treatment scale up. An effective model to support HIV scale-up decisions will be flexible, with capability for parameter customization and incorporation of uncertainty. Such a model needs certain key technical features: it must capture epidemic effects; account for how intervention effectiveness depends on the target population and the level of scale up; capture benefit and cost differentials for packages of interventions versus single interventions, including both treatment and prevention interventions; incorporate key constraints on potential funding allocations; identify optimal or near-optimal solutions; and estimate the impact of HIV interventions on the health care system and the resulting resource needs. Additionally, an effective model needs a user-friendly design and structure, ease of calibration and validation, and accessibility to decision makers in all settings. Resource allocation theory can make a significant contribution to decision making about HIV prevention and treatment scale up. What remains now is to develop models that can bridge the gap between theory and practice.


Editors’ note: This helpful review describes the variety of modelling approaches that have been developed since the field of resource allocation for epidemic control became a topic of interest in the 1920s. It focuses on three broad categories of models (linear, dynamic, and simulation), providing examples of each from the HIV prevention literature. Issues that models often do not address include the impact of joint interventions on HIV infections averted—not additive because you cannot prevent the same HIV infection twice—decreasing/increasing returns to scale, allocation of resources to treatment programmes, ethical and equity concerns, human and financial resource implications for the entire healthcare system, and being user-
friendly for decision-makers. A practical resource allocation model would have input flexibility, pertinent technical capabilities, and usability—the challenge now is to translate the theory into practice. The time is ripe—good investment decisions are essential to reap returns.

11. People who inject drugs

Drug Arrests and Injection Drug Deterrence


Friedman and colleagues tested the hypothesis that higher rates of previous hard drug-related arrests predict lower prevalence of injection drug use. They analyzed drug-related arrest data from the Federal Bureau of Investigation’s Uniform Crime Reporting Program for 93 large US metropolitan statistical areas in 1992 to 2002 to predict previously published annual estimates of the number of people who inject drugs per 10,000 population. In linear mixed-effects regression, hard drug-related arrest rates were positively associated (parameter=+1.59; SE=0.57) with the population prevalence of people who inject drugs in 1992 and were not associated with change in the prevalence of people who inject drugs over time (parameter = -0.15; SE=0.39). Deterrence-based approaches to reducing drug use seem not to reduce the prevalence of people who inject drugs. Alternative approaches such as harm reduction, which prevents HIV transmission and increases referrals to treatment, may be a better foundation for policy.


Editors’ note: This is an important topic for the USA where drug-related incarceration rates are 8 times higher for African-Americans compared to Whites, with shortages of men in some African-American communities contributing to family breakdown. This ecological study using non-experimental data provides no support for the idea that punishment and stigmatization through arrest will deter people from injecting drugs. Theoretically, if deterrence works then increasing arrest rates should be followed by decreased drug injecting and decreasing arrest rates should be followed by increasing drug use. The study attempted to control for potential confounders such as economic context and social cohesion. The results raise questions about criminal deterrence theory and suggest that greater effort needs to be invested in reinforcing public health approaches to injecting drug use if HIV-related consequences are to be minimized.

12. Preventing vertical transmission

Mother to child transmission of HIV among Zimbabwean women who seroconverted postnatally: prospective cohort study


Humphrey and colleagues estimated the rates and timing of mother to infant transmission of HIV associated with breastfeeding in mothers who seroconvert postnatally, and their breast milk and plasma HIV loads during and following seroconversion, compared with women who tested HIV positive at delivery. This prospective cohort study that enrolled 14,110 women and infants in the Zimbabwe Vitamin A for Mothers and Babies (ZVITAMBO) trial (1997-2001) also assessed postnatal mother to child transmission of HIV and collected information on breast milk and maternal plasma HIV load during the postpartum period. Among mothers who tested HIV positive at baseline and whose infant tested HIV negative with polymerase chain reaction (PCR) at six weeks (n=2870), breastfeeding associated transmission was responsible for an average of 8.96 infant infections per 100 child years of breastfeeding (95% CI 7.92 to 10.14) and varied little over the breastfeeding period. Breastfeeding associated transmission for mothers who
seroconverted postnatally (n=334) averaged 34.56 infant infections per 100 child years (95% CI 26.60 to 44.91) during the first nine months after maternal infection, declined to 9.50 (95% CI 3.07 to 29.47) during the next three months, and was zero thereafter. Among women who seroconverted postnatally and in whom the precise timing of infection was known (<90 days between last negative and first positive test; n=51), 62% (8/13) of transmissions occurred in the first three months after maternal infection and breastfeeding associated transmission was 4.6 times higher than in mothers who tested HIV positive at baseline and whose infant tested HIV negative with PCR at six weeks. Median plasma HIV concentration in all mothers who seroconverted postnatally declined from 5.0 log(10) copies/mL at the last negative enzyme linked immunosorbent assay (ELISA) to 4.1 log(10) copies/mL at 9-12 months after infection. Breast milk HIV load in this group was 4.3 log(10) copies/mL 0-30 days after infection, but rapidly declined to 2.0 log(10) copies/mL and <1.5 log(10) copies/mL by 31-90 days and more than 90 days, respectively. Among women whose plasma sample collected soon after delivery tested negative for HIV with ELISA but positive with PCR (n=17), 75% of their infants were infected or had died by 12 months. An estimated 18.6% to 20.4% of all breastfeeding associated transmission observed in the ZVITAMBO trial occurred among mothers who seroconverted postnatally. Breastfeeding associated transmission is high during primary maternal HIV infection and is mirrored by a high but transient peak in breast milk HIV load. Around two thirds of breastfeeding associated transmission by women who seroconvert postnatally may occur while the mother is still in the “window period” of an antibody based test, when she would test HIV negative using one of these tests.


Editors’ note: The ZVITAMBO trial is the largest vertical HIV transmission trial ever reported and although it found that Vitamin A supplements did not prevent mother-to-child transmission, it is a rich source of data. This study found that 8.5% of infants born without HIV to chronically HIV-infected women became infected through breastfeeding during the first year of life, a risk that was constant over time. Infants of women who were HIV-negative at delivery and subsequently seroconverted while breastfeeding had a 23.6% risk of acquiring HIV by 12 months. Just as in sexual transmission, very high rates of transmission were seen during the acute infection period, with the transmission rate among postnatal seroconverter women 8 times the transmission risk of chronically infected women. During the first 30 days of acute infection, the median breast milk viral load peaked in the same range as plasma viral load. What conclusion can we draw? The WHO infant feeding guidelines on maternal antiretroviral prophylaxis or therapy while breastfeeding and infant prophylaxis will not address this problem because these women would not be offered this strategy—they seroconverted after delivery. Even monthly HIV antibody testing following delivery would not identify women in the acute infection period when they are most likely to transmit. Only preventing HIV acquisition in women—primary prevention—will address this. This is a cogent argument for including breastfeeding women in high HIV prevalence areas in topical and oral pre-exposure prophylaxis trials. In the meantime, it is important to spread the word that pregnancy and breastfeeding are times of increased risk of HIV acquisition for women and that correct and consistent condom use by men who have sex with them will protect their infants and reduce the risk that they may become eventual maternal orphans.

13. Men who have sex with men

Ongoing HIV-1 transmission among men who have sex with men in Amsterdam: a 25-year prospective cohort study


To examine the suggested resurgence of the HIV epidemic among men who have sex with men, Jansen and colleagues studied trends in HIV-1 incidence rates, sexual risk behaviour, risk factors for HIV-1 seroconversion, and source of HIV-1 infection among men who have sex with men in the Amsterdam Cohort Studies from 1984 to 2009. Trends in HIV-1 incidence and risk factors for HIV-1 infection were studied using Poisson regression. Trends in sexual risk behaviour were evaluated using logistic regression, correcting for
intra-individual correlation via generalized estimating equations. Trends in the source of HIV-1 infection were modelled via logistic regression. Of 1642 HIV-1-negative individuals, 217 seroconverted during follow-up. HIV-1 incidence rates strongly decreased from 8.6/100 person-years in 1985 to 1.3/100 person-years in 1992; remained relatively stable around 1.0/100 person-years between 1992 and 1996, and slowly increased to 2.0/100 person-years in 2009 (P = 0.14; linear trend 1996-2009). Reports of unprotected anal intercourse increased significantly from 1996 onwards. HIV-1 seroconversion was associated with receptive unprotected anal intercourse with casual partners, more than five sexual partners, a history of gonorrhoea (all in the preceding 6 months), and a lower educational level. Currently, men who have sex with men are more likely to have contracted HIV-1 from casual partners than from steady partners, but trends of recent years suggest that steady partners became a growing source with increasing age. Following increases in sexual risk behaviour from 1996 onwards, HIV-1 continues to spread among men who have sex with men. Targeted prevention messages should continue to focus on sexual behaviour with casual partners, but also on sexual behaviour within steady relationships.


Editors’ note: The Amsterdam Cohort Studies (ACS) recently achieved 25 years of follow-up documenting changes over this period in behavioural risk and HIV incidence in men who have sex with men. The proportion of men reporting unprotected anal intercourse in the preceding 6 months decreased from 78% in 1984 to 33% in 1988 before increasing to 38% in 1995 and 55% in 2009. Men were more likely to practice unprotected anal intercourse after the introduction of combination antiretroviral therapy in 1996 than in the 5 years prior, a trend seen with both casual and steady partners. HIV incidence has remained relatively stable increasing from 1.4 per 100 person years in 1996 to 2.0 per 100 person years in 2009. Other national and international studies in the North are reporting increases in sexually transmitted diseases and new diagnoses of HIV infection among men who have sex with men, reinforcing the need for sustained HIV prevention strategies. The data from AMC suggest that these should focus on reducing risk with both casual and steady partners.

14. Ethics

The challenge of defining standards of prevention in HIV prevention trials


As new HIV prevention tools are developed, researchers face a number of ethical and logistic questions about how and when to include novel HIV prevention strategies and tools in the standard prevention package of ongoing and future HIV prevention trials. Current Joint United Nations Programme on HIV/AIDS (UNAIDS)/World Health Organization (WHO) guidance recommends that participants in prevention trials receive 'access to all state of the art HIV risk reduction methods', and that decisions about adding new tools to the prevention package be made in consultation with 'all relevant stakeholders'. The guidance, however, leaves open questions of both process and implementation. In March 2009, the Global Campaign for Microbicides, UNAIDS, and the Centers for Disease Control and Prevention convened a consultation to develop practical answers to these questions. Fifty-nine diverse participants, including researchers, ethicists, advocates, and policymakers, worked to develop consensus criteria on when to include new HIV prevention tools in future trials. Participants developed a set of questions to guide decision-making, including: whether the method has been recommended by international bodies or adopted at a national level; the size of the effect and weight of the evidence; relevance to the trial population; whether the tool has been approved or introduced in the trial country; whether adding the tool might lead to trial futility; outstanding safety issues and status of the trial. Further work is needed to develop, implement and evaluate approaches to facilitate meaningful stakeholder participation in this deliberative process.

Editors’ note: Biomedical HIV prevention is an evolving field with 3 African trials of male circumcision, the Thai RV144 vaccine trial, the CAPRISA 004 tenofovir gel trial, and the iPrEx trial of pre-exposure prophylaxis among men who have sex with men—all having reported encouraging results. Offering male circumcision to heterosexual men participating in HIV prevention trials in high HIV prevalence settings is now considered standard of prevention. What of the other trials that provided proof-of-concept that a vaccine could work, that gel use could protect, and that antiretroviral pill-taking prevents HIV acquisition? This article highlights the thorny issues that researchers, sponsors, funders, communities, ethicists, advocates, and government decision makers must face in deciding together what prevention services should be offered to all trial participants. We can expect an even more complicated situation over the coming 3 years as more trials of topical and oral pre-exposure prophylaxis report findings in diverse populations.

15. Microbicides

Female genital tract secretions and semen impact the development of microbicides for the prevention of HIV and other sexually transmitted infections


Pharmacologic strategies for the prevention of HIV include vaccines, post-exposure prophylaxis with antiretroviral therapy, and topical microbicides. Vaginal microbicides have the potential to augment innate defenses in the genital tract but may also disrupt endogenous protection and increase HIV acquisition risk, as observed in clinical trials of nonoxynol-9. The initially disappointing results of microbicide clinical trials stimulated the development of more sensitive and comprehensive pre-clinical safety studies, which include dual-chamber culture systems to model the epithelial barrier and post-coital studies to evaluate the effects of semen and sexual intercourse on microbicide efficacy. This review discusses the key factors that contribute to a healthy female genital tract environment, the impact of semen on mucosal defense, and how our understanding of these mediators informs the development of effective vaginal microbicides.


Editors’ note: This article provides strong justification for conducting pharmacokinetic and pharmacodynamic studies for microbicide candidates using post-coital samples rather than ordinary cervicovaginal secretions. The female genital tract has several natural host defences that semen counteracts. It neutralises the protective acidic pH of vaginal fluid, stimulates inflammatory cytokines, and causes white cells and Langerhans cells to come into the path of HIV. More directly, semen contains prostatic acid phosphatise which forms fibrils that capture HIV and help their attachment to target cells. Semen may also interfere with defensins, SLPI (secretory leukocyte protease inhibitor), and other antimicrobial proteins found in cervicovaginal secretions. Clearly, when we are trying to measure the effects of a microbicide candidate on the multilayered squamous epithelial barrier of the vagina we have to include semen. Predictive safety assays such as those described in this article are helping us understand why microbicide candidates such as non-oxynol 9 and cellulose sulfate increased risk of HIV acquisition. We need to better understand mucosal immunity and the role of semen in order to find ways to increase women’s natural defenses. In the meantime, reading this article brings the reader right back to square one—if there is any possibility of HIV or genital herpes, use a condom if you are not trying to get pregnant!

16. Nutrition

Micronutrient supplementation in children and adults with HIV infection

Irlam JH, Visser MM, Rollins NN, Siegfried N. Cochrane Database Syst Rev. 2011, Issue 2. CD003650

Editors’ note: This article provides strong justification for conducting pharmacokinetic and pharmacodynamic studies for microbicide candidates using post-coital samples rather than ordinary cervicovaginal secretions. The female genital tract has several natural host defences that semen counteracts. It neutralises the protective acidic pH of vaginal fluid, stimulates inflammatory cytokines, and causes white cells and Langerhans cells to come into the path of HIV. More directly, semen contains prostatic acid phosphatise which forms fibrils that capture HIV and help their attachment to target cells. Semen may also interfere with defensins, SLPI (secretory leukocyte protease inhibitor), and other antimicrobial proteins found in cervicovaginal secretions. Clearly, when we are trying to measure the effects of a microbicide candidate on the multilayered squamous epithelial barrier of the vagina we have to include semen. Predictive safety assays such as those described in this article are helping us understand why microbicide candidates such as non-oxynol 9 and cellulose sulfate increased risk of HIV acquisition. We need to better understand mucosal immunity and the role of semen in order to find ways to increase women's natural defenses. In the meantime, reading this article brings the reader right back to square one—if there is any possibility of HIV or genital herpes, use a condom if you are not trying to get pregnant!
Micronutrient deficiencies are widespread and compound the effects of HIV disease; micronutrient supplements may be effective and safe in reducing this burden. To assess whether micronutrient supplements are effective and safe in reducing mortality and morbidity in adults and children with HIV infection, the CENTRAL, EMBASE, PubMed, and GATEWAY databases were searched for randomised controlled trials of micronutrient supplements using the search methods of the Cochrane HIV/AIDS Group. Randomised controlled trials were selected that compared the effects of micronutrient supplements (vitamins, trace elements, and combinations of these) with other supplements, placebo or no treatment on mortality, morbidity, pregnancy outcomes, immunologic indicators, and anthropometric measures in HIV-infected adults and children. Any adverse effects of supplementation were recorded. Two reviewers independently selected trials, appraised trial quality for risk of bias using standardised criteria, and extracted data using standardised forms. Sixteen additional trials are included in this update to the original Cochrane review (Irlam 2005). Overall, 30 trials involving 22,120 participants are reviewed: 20 trials of single supplements (vitamin A, vitamin D, zinc, selenium) and 10 of multiple micronutrients. Eight trials were undertaken in child populations. None of the six trials of vitamin A or beta-carotene supplementation in adults demonstrated any significant reduction in HIV disease progression. Vitamin A halved all-cause mortality in a meta-analysis of three trials in African children, had inconsistent impacts on diarrhoeal and respiratory morbidity, and improved short-term growth in one trial. No significant adverse effects of vitamin A in adults or children have been reported. Zinc supplements reduced diarrhoeal morbidity and had no adverse effects on disease progression in a single safety trial in South African children. No significant clinical benefits were found from zinc supplementation of pregnant Tanzanian women or Peruvian adults with persistent diarrhoea. Selenium reduced diarrhoeal morbidity in pregnant women in Tanzania, and reduced viral load in two separate small trials in American adults. Single trials of vitamin D supplements in adults, and in adolescents and children, demonstrated safety but no clinical benefits. Multiple micronutrient supplements conferred multiple clinical benefits to pregnant women and their offspring in a large Tanzanian trial. Supplementation in another Tanzanian trial reduced the recurrence of pulmonary tuberculosis and increased weight gain in co-infected patients. No significant adverse effects were reported. Multiple micronutrient supplements reduced morbidity and mortality in HIV-infected pregnant women and their offspring and also improved early child growth in one large randomised controlled trial in Africa. Additional research is needed to determine if these are generalisable findings. Vitamin A supplementation is beneficial and safe in HIV-infected children, but further evidence is needed to establish if supplementation confers similar benefits in HIV-infected adults. Zinc is safe in HIV-infected adults and children. It may have similar benefits in HIV-infected children and adults, and uninfected children with diarrhoea, as it does in HIV-uninfected children. Further trials of single supplements (vitamin D, zinc, and selenium) are required to build the evidence base. The long-term clinical benefits, adverse effects, and optimal formulation of multiple micronutrient supplements require further investigation in individuals with diverse disease status.


Editors’ note: Priority interventions to reduce child mortality in resource-constrained settings include Vitamin A supplementation 6-monthly, zinc supplementation as part of diarrhoea management, multiple micronutrient supplementation for children in non-malaria regions and improved iron intake by young children in malaria regions, and iron and folic supplementation for all women of childbearing age with a focus on pregnant and breastfeeding women. In areas with endemic micronutrient deficiencies, food fortification and micronutrient supplementation can benefit the entire population. This review found a limited evidence base for the specific effects of micronutrient supplementation in children and adults with HIV infection, other than that already recommended. Observational studies suggest that both protein-energy malnutrition and micronutrient deficiencies can hasten HIV disease progression while HIV infection itself can worsen malnutrition. Antiretroviral therapy breaks this vicious cycle, improving nutritional status but, to give treatment a chance to work, food supplementation during treatment initiation is needed for some adults and children. The efficacy, safety, and short- and long-term benefits of some single and multiple micronutrient
supplements in people living with HIV will not be demonstrated without adequately powered studies – prime candidates for study would be selenium, vitamin D, and zinc.

17. Comorbidities, tuberculosis

The effect of tuberculosis on mortality in HIV positive people: a meta-analysis


Tuberculosis is a leading cause of death in people living with HIV. Straetemans and colleagues conducted a meta-analysis of cohort studies to assess the effect of tuberculosis on mortality in people living with HIV. To identify eligible studies, the authors systematically searched electronic databases (until December 2008), performed manual searches of citations from relevant articles, and reviewed conference proceedings. Multivariate hazard ratios of mortality in people living with HIV with and without tuberculosis, estimated in individual cohort studies, were pooled using random effect weighting according to “Der Simonian Laird method” if the p-value of the heterogeneity test was <0.05. **Fifteen cohort studies** were systematically retrieved. Pooled overall analysis of these 15 studies estimating the effect of tuberculosis on mortality in people living with HIV showed a hazard ratio of 1.8 (95% confidence interval (CI): 1.4-2.3). Subanalysis of 8 studies in which the cohort was not exposed to highly active antiretroviral therapy showed a hazard ratio of 2.6 (95% CI: 1.8-3.6). Subanalysis of 6 studies showed that tuberculosis did not show an effect on mortality in people living with HIV exposed to antiretroviral therapy, hazard ratio 1.1 (95% CI: 0.9-1.3). These results provide an indication of the magnitude of benefit to an individual that could have been expected if tuberculosis had been prevented. It emphasizes the need for additional studies assessing the effect of preventing tuberculosis or early diagnosis and treatment of tuberculosis in people living with HIV on reducing mortality. Furthermore, the results of the subgroup analyses in cohorts largely exposed to antiretroviral therapy provide additional support to WHO's revised guidelines, which include promoting the initiation of antiretroviral therapy for people living with HIV co-infected with tuberculosis. The causal effect of tuberculosis on mortality in people living with HIV exposed to antiretroviral therapy needs to be further evaluated once the results of more cohort studies become available.


**Editors’ note:** Given that people living with HIV in countries with an HIV prevalence above 1% are estimated to have a 20-fold risk of developing tuberculosis disease, early detection and treatment of TB disease is important to survival. However detection is complicated by the fact that people living with HIV often have atypical symptoms, are more likely to have negative sputum smears with pulmonary TB, and are more likely to have extrapulmonary TB. This meta-analysis found that people who have HIV infection and TB face a 2-fold higher risk of mortality from all causes compared to people living with HIV who do not have TB. Isoniazid preventive therapy for people diagnosed with HIV infection and infection control measures to reduce the spread of TB in clinical settings are two important measures. Further, intensified case finding to actively identify TB in people living with HIV and initiate treatment can help reduce both mortality and TB spread. These are the three ‘Is’: isoniazid, infection control, and intensified case finding.

18. Child-led microfinance

Community relations and child-led microfinance: a case study of caregiving children in Kenya

*Skovdal M. AIDS Care. 2010;22 Suppl 2:1652-61*

Rampant levels of AIDS and poverty have made many children in sub-Saharan Africa the primary caregivers of their ageing or ailing guardians. This paper reports on a social action fund initiative that brought caregiving children together to set up and run income generating activities as a group with
the aim of strengthening their coping capabilities. To further our understanding of child-led microfinance activities, this paper explores how intra-community relations can both facilitate and undermine child-led activities, and how these activities in turn can further strengthen some intra-community relations. Twenty-one children (aged 12-17) and six guardians participated in this study. Data included draw-and-write compositions (n=21), essays (n=16), workshop notes and proposals (n=8) and in-depth interviews (n=16). A thematic analysis revealed that the children actively drew on the expertise and involvement of some guardians in the project as well as on each other, developing supportive peer relations that helped strengthen their coping capabilities. However, the children's disenfranchised position in the community meant that some adults took advantage of the child-led activities for their own personal gain. Some children also showed a lack of commitment to collective work, undermining the morale of their more active peers. Nevertheless, both guardians and the children themselves began to look at caregiving children differently as their engagement in the project began to earn them respect from the community - changing guardian/child relations. The paper concludes that microfinance interventions targeting children and young people must consider children's relationships with each other and with adults as key determinants of project success.


Editors’ note: This interesting report describes the involvement and perspectives of caregiving children in a participatory microfinance programme. The sample size was small and self-selected since only children who wanted to share their experiences gave their views. However, the social action fund activities that they were involved in appeared to enhance their social status, their confidence, and their sense of agency. A clear lesson was the importance of intra-community relations in both facilitating and hindering the children’s project, suggesting the importance of community buy-in to child-led microfinance. This new area of research is aimed at evaluating the results of social action fund initiatives in furthering children’s empowerment and enhancing their skills and social, political, and financial resources to cope with adversity.

That was HIV this week, signing off.

Editors’ notes on journal access

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