Welcome to the 66th issue of HIV This Week! In this issue, we cover, cost-effectiveness (four HIV counselling and testing strategies get compared), disclosure (test and tell in South Africa; Ubuntu and confidentiality among the Bantu), basic science (glycerol monolaurate is a story to follow), positive prevention (the virus stops with me in Uganda), gender (why bother with younger men: the attraction of age-disparate sex in southern Africa; HIV-positive pregnant women bear the brunt of intimate partner violence in Rwanda), infant survival (why breastfeeding is the only choice in rural Africa; loss to follow-up is a real concern in paediatric HIV treatment programmes), structural determinants (young women and economic empowerment for HIV prevention; preventing treatment interruptions during Kenya’s post-election violence), food insecurity (a trailblazing nutrition support programme lights the path forward; an interactive approach to solving food insecurity is challenged by HIV), treatment (stocktaking on women and antiretroviral drugs; 25 compounds in 25 years; higher mortality among young or unemployed men on antiretroviral treatment in Nigeria), comorbidities (striking levels of anal human papillomavirus infection and anal cancer in women), reproductive health and HIV (strong correlations between antiretroviral treatment and contraceptive use in Mbarara, Uganda; why and how reproductive health services should be integrated into antiretroviral treatment programmes), sexual transmission (did intensive HIV prevention programmes for sex workers bring down general population HIV prevalence in Karnataka, India?), barrier protection (some men do help with the female condom; product substitution in the MIRA diaphragm trial), and vaccines (AIDSVAX reveals another twist in the CD8+ T-cell response story).

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1. **Cost-effectiveness**


HIV counselling and testing is a key intervention for HIV control, and new strategies have been developed for expanding coverage in developing countries. Menzies and colleagues compared costs and outcomes of four HIV counselling and testing strategies in Uganda. A retrospective cohort of 84,323 individuals received HIV counselling and testing at one of four Ugandan HIV counselling and testing programmes between June 2003 and September 2005. Strategies assessed were stand-alone; hospital-based; household-member; and door-to-door. The authors collected data on client volume, demographics, prior testing and HIV diagnosis from project monitoring systems, and cost data from project accounts and personnel interviews. Strategies were compared in terms of costs and effectiveness at reaching key population groups. Household-member and door-to-door HIV counselling and testing strategies reached the largest proportion of previously untested individuals (>90% of all clients). Hospital-based HIV counselling and testing diagnosed the greatest proportion of HIV-infected individuals (27% prevalence), followed by stand-alone HIV counselling and testing (19%). Household-member HIV counselling and testing identified the highest percentage of discordant couples; however, this was a small fraction of total clients (<4%).

Costs per client (2007 USD) were $19.26 for stand-alone, $11.68 for hospital-based, $13.85 for household-member, and $8.29 for door-to-door- HIV counselling and testing. All testing strategies had relatively low per client costs. Hospital-based HIV counselling and testing most readily identified HIV-infected individuals eligible for treatment, whereas home-based strategies more efficiently reached populations with low rates of prior testing and HIV-infected people with higher CD4 cell counts. Multiple HIV counselling and testing strategies with different costs and efficiencies can be used to meet the UNAIDS/WHO call for universal HIV counselling and testing access by 2010.

Editors' note: This useful cost-effectiveness study of four different HIV counselling and testing strategies that a national HIV programme might consider demonstrates the value of each in a generalized epidemic. More than 30 per cent (range 30.7-48.1 per cent) of all people found HIV-positive had advanced immunosuppression (CD4+ count <200 cells/μl) regardless of testing strategy. Door-to-door strategies reached previously untested people cheaply in this country where in 2007 less than a quarter of people had ever been tested. These data indicate that a variety of testing strategies, providing choices for individuals, couples, and communities, can work in complementary fashion to accomplish the goals of increasing knowledge of serostatus and facilitating earlier treatment initiation.

2. **Disclosure**


As the numbers of HIV-positive diagnoses rise in South Africa, it is important to understand the determinants and consequences of HIV disclosure. Wong and colleagues conducted a cross-sectional survey from random community samples of men and women in urban and rural South Africa (n = 217 HIV-positive individuals, 89% female). Two thirds of all known HIV-
infected adults in these communities had disclosed their status to sexual partner(s). On average, individuals who disclosed were 2 years older, higher in socioeconomic assets, and had known their HIV status 7 months longer than those who had not told their sexual partner(s). The "need for privacy" was the most cited reason (45%) for nondisclosure among those who had never disclosed. People who eventually disclosed their HIV status to sexual partner(s) were significantly more likely to report always or more frequently using condoms, reducing their number of sexual partners, and/or becoming monogamous. Among individuals who disclosed their HIV status, 77% reported increases in social support, with families providing the most support. The authors concluded that disclosure is associated with reports of consequent safer sexual behaviour and greater social support. Interventions might be informed by the costs and benefits of disclosure and differences in disclosure to sexual partner compared to one's social network.

Editors' note: While most studies of disclosure to date have been clinic-based, this is the first community study to examine HIV disclosure in South Africa. Conducted in 2003, the study found that, although 87% of HIV-positive individuals had disclosed their status to at least one person, more than a third did not disclose to sex partners. Since both sexual behaviour change and receiving more social support were associated with disclosure, further study of the barriers and facilitators of disclosure can help design programmes to assist people in making decisions about revealing their serostatus.


The principle of individual medical confidentiality is one of the moral principles that Africa inherited unquestioningly from the West as part of Western medicine. The HIV pandemic in Southern Africa has reduced the relevance of the principle of individual medical confidentiality. Individual medical confidentiality has especially presented challenges for practitioners among the Bantu communities that are well known for their social interconnectedness and the way they value their extended family relations. Individual confidentiality has raised several unforeseen problems for persons living with HIV, ranging from stigma and isolation to feelings of dejection as it drives them away from their families as a way of trying to keep information about their conditions confidential. The involvement of family members in treatment decisions is in line with the philosophy of Ubuntu and serves to respect patients' and families' autonomy while at the same time benefiting the individual patient.

Editors' note: Regardless of location worldwide, respect for patients and for their cultural context should translate into careful consultation with them to obtain their consent for the involvement of family members. For rural Bantu-speaking people in Central, Eastern and Southern Africa where communitarian values are still dominant, the prevailing philosophy of Ubuntu represents group solidarity, compassion and mutual support that people living with HIV can draw down on and contribute to once they decide to share knowledge of their HIV infection.

3. **Basic science**

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Although there has been great progress in treating human immunodeficiency virus 1 (HIV-1) infection, preventing transmission has thus far proven an elusive goal. Indeed, recent trials of a candidate vaccine and microbicide have been disappointing, both for want of efficacy and concerns about increased rates of transmission. Nonetheless, studies of vaginal transmission in the simian immunodeficiency virus (SIV)-rhesus macaque (Macaca mulatta) model point to opportunities at the earliest stages of infection in which a vaccine or microbicide might be protective, by limiting the expansion of infected founder populations at the portal of entry. Here Li and colleagues show in this SIV-macaque model, that an outside-in endocervical mucosal signalling system, involving MIP-3 (also known as CCL20), plasmacytoid dendritic cells and CCR5 cell-attracting chemokines produced by these cells, in combination with the innate immune and inflammatory responses to infection in both cervix and vagina, recruits CD4 T cells to fuel this obligate expansion. They then show that glycerol monolaurate—a widely used antimicrobial compound with inhibitory activity against the production of MIP-3a and other proinflammatory cytokines—can inhibit mucosal signalling and the innate and inflammatory response to HIV-1 and SIV in vitro, and in vivo it can protect rhesus macaques from acute infection despite repeated intra-vaginal exposure to high doses of SIV. This new approach, plausibly linked to interfering with innate host responses that recruit the target cells necessary to establish systemic infection, opens a promising new avenue for the development of effective interventions to block HIV-1 mucosal transmission.

Editors' note: This study reveals that the endocervix, the inner surface of the cervix linking the vagina with the uterus or womb, is the predominant site for initial infected cell clusters. There are not enough target cells there for SIV infection to take hold but the inflammatory response of the innate mucosal immune system calls more target cells to this site, expanding the infected founder cell population which then allows establishment of self-propagating infection in lymph tissues. In this encouraging report, inexpensive and safe glycerol monolaurate brakes this vicious cycle of signalling and inflammatory response to prevent acute SIV infection in several repeatedly exposed animals. Longer-term and well-powered studies with larger numbers of animals are clearly warranted.

4. Positive prevention


Few Positive Prevention interventions have been implemented in Africa; however, greater attention is now being paid to interventions that include messages of personal responsibility or altruism that may motivate HIV-infected individuals towards HIV prevention behaviours in Africa. King and colleagues conducted 47 in-depth interviews in 2004 with HIV-infected men and women purposefully sampled to represent a range of sexual activities among clients of an AIDS support organization in Uganda. Qualitative interviews were selected from a cross-sectional survey of 1092 HIV-infected men and women. Clients were interviewed about their concerns around sexual HIV transmission, feelings of responsibility and reasons for these feelings, as well as about the challenges and consequences of actions to prevent HIV
transmission. The reasons they provided for their sense of prevention responsibility revolved around ethical and practical themes. Responsibility toward sexual partners was linked to the belief that conscious transmission of HIV equals murder, would cause physical and emotional harm, and would leave children orphaned. The primary reason specific to preventing HIV transmission to unborn children was the perception that they are ‘innocent’. Most participants felt that HIV-infected individuals held a greater responsibility for preventing HIV transmission than did HIV-uninfected individuals. Respondents reported that their sense of responsibility lead them to reduce HIV transmission risk, encourage partner testing, disclose HIV test results, and assume an HIV educator role. Challenges to HIV preventive behaviour and altruistic intentions included: sexual desire; inconsistent condom use, especially in long term relationships; myths around condom use; fear of disclosure; gender-power dynamics; and social and financial pressure. The authors’ finding that altruism played an important role in motivating preventive behaviours among HIV-infected persons in Uganda supports the inclusion of altruistic prevention and counselling messages within Positive Prevention interventions.

Editors’ note: People living with HIV play a critical role in stopping HIV transmission. Studies such as these that determine the personal motivators for prevention and explore the barriers and facilitators for people living with HIV can help reinvigorate prevention messages in counselling. They shift the prevention focus to empowering people with HIV infection to prevent transmission to sexual partners and unborn children.

5. Gender


Leclerc-Madlala reviews the current state of knowledge on age-disparate sexual relationships in the context of the southern African HIV hyperepidemic. Disproportionately high HIV infection rates among young women aged 15-24 years have been attributed to their greater involvement in relationships with older-aged partners. Whereas early studies emphasized economic concerns in the context of poverty as driving girls to accept or seek the attentions of older employed men, close-grained studies reveal a complex interplay of meanings and motives that prompt both men and women across socioeconomic strata to engage in intergenerational sex. Studies have revealed that age-disparate relationships are meaningful and perceived as beneficial at a number of levels, including social, physical, psychological, as well as economic and symbolic. In the context of growing economic inequalities and cultural expectations for men to give and women to receive a compensation for sex, relationships with older men are a common and readily available way through which young women gain materially, affirm self-worth, achieve social goals, increase longer-term life chances, or otherwise add value and enjoyment to life. Awareness of HIV risks in these relationships remains low. HIV prevention policies and programmes need to start from an understanding of how those engaged in risky behaviour perceive their sexual relationships and conceptualize the choices they make and the strategies they use. A more comprehensive policy on women and girls with better integration of communities in assessing and addressing issues, and an expansion of campaigns and programmes on the role of men as protectors and supporters of women are recommended.
Editors' note: This excellent review describes the facilitating social factors in both rural and urban settings that may motivate younger women to value age-disparate sexual relationships for their potential to provide access to social, emotional, symbolic, and financial capital. While young women often hold positive perceptions toward age-disparate relationships, they are aware of the dangers of dependency and unsafe sex leading to pregnancy and sexually transmitted infections including HIV. Although they may be pushed into sexual liaisons with older men for survival reasons, many young women do not perceive themselves as victims. Acknowledging the implicit transactional and reciprocal elements of age-disparate sex and the wider realities of women’s lives in southern Africa is fundamental to a two-pronged approach that focuses on empowering women while working to change men’s behaviours and attitudes. In communities most at risk, creative ways need to be found to support male champions for HIV prevention who represent a masculinity that protects self and others from HIV.


Intimate partner violence, defined as actual or threatened physical, sexual, psychological, and emotional abuse by current or former partners is a global public health concern. The prevalence and determinants of intimate partner violence against pregnant women has not been described in Rwanda. A study was conducted to identify variables associated with intimate partner violence among Rwandan pregnant women. A convenient sample of 600 pregnant women attending antenatal clinics were administered a questionnaire which included items on demographics, HIV status, intimate partner violence, and alcohol use by the male partner. Mean age and proportions of intimate partner violence in different groups were assessed. Odds of intimate partner violence were estimated using logistic regression analysis. Of the 600 respondents, 35.1% reported intimate partner violence in the last 12 months. HIV-positive pregnant women had higher rates of all forms of intimate partner violence than HIV-negative pregnant women: pulling hair (44.3% vs. 20.3%), slapping (32.0% vs. 19.7%), kicking with fists (36.3% vs. 12.7%), and burning with hot liquid (4.1% vs. 3.5%). HIV-positive participants were more than twice likely to report physical intimate partner violence than those who were HIV-negative (OR = 2.38; 95% CI [1.59, 3.57]). Other factors positively associated with physical intimate partner violence included sexual abuse before the age of 14 years (OR = 2.69; 95% CI [1.69, 4.29]), having an alcohol drinking male partner (OR = 4.10; 95% CI [2.48, 6.77] for occasional drinkers and OR = 3.37; 95% CI [2.05, 5.54] for heavy drinkers), and having a male partner with other sexual partners (OR = 1.53; 95% CI [1.15, 2.20]. Education was negatively associated with lifetime intimate partner violence. In reporting on prevalence of intimate partner violence among pregnant women attending antenatal care in Rwanda, Central Africa, the authors advocate that screening for intimate partner violence be an integral part of HIV care, as well as routine antenatal care. Services for battered women should also be made available.

Editors' note: Intimate partner violence affects 25-43% of women globally at some point in their lifetime. That over one-third of pregnant women and almost one-half of HIV-positive pregnant women in this Rwandan study had experienced such violence in the past 12 months is striking. In addition to the significant mental and physical health consequences for women, physical violence increases the risk of low birth weight.
infants, pre-term delivery and neonatal death, and negatively affects breast feeding post partum. Prenatal care providers should have a high degree of suspicion of intimate partner violence among pregnant women with HIV infection and make a concerted effort to provide necessary social, treatment, and legal support for these women.

6. Infant survival


Data comparing survival of formula-fed to breast-fed infants in programmatic settings are limited. Kagaayi and colleagues compared mortality and HIV-free of breast and formula-fed infants born to HIV-positive mothers in a program in rural, Rakai District Uganda. 182 infants born to HIV-positive mothers were followed at one, six and twelve months postpartum. Mothers were given infant-feeding counselling and allowed to make informed choices as to whether to formula-feed or breast-feed. Eligible mothers and infants received antiretroviral therapy if indicated. Mothers and their newborns received prophylaxis for prevention of mother-to-child HIV transmission (pMTCT) if they were not receiving antiretroviral therapy. Infant HIV infection was detected by polymerase chain reaction (Roche Amplicor 1.5) during the follow-up visits. Kaplan-Meier time-to-event methods were used to compare mortality and HIV-free survival. The adjusted hazard ratio (Adjusted HR) of infant HIV-free survival was estimated by Cox regression. Seventy-five infants (41%) were formula-fed while 107 (59%) were breast-fed. Exclusive breast feeding was practiced by only 25% of breast-feeding women at one month postpartum. The cumulative 12-month probability of infant mortality was 18% (95% CI = 11%-29%) among the formula-fed compared to 3% (95% CI = 1%-9%) among the breast-fed infants (unadjusted hazard ratio (HR) = 6.1(95% CI = 1.7-21.4, P-value<0.01). There were no statistically significant differentials in HIV-free survival by feeding choice (86% in the formula-fed compared to 96% in breast-fed group (Adjusted HR = 2.8[95%CI = 0.67-11.7, P-value = 0.16]. Formula feeding was associated with a higher risk of infant mortality than breastfeeding in this rural population. The authors conclude that these findings suggest that formula feeding should be discouraged in similar African settings.

Editors' note: This small study in which women self-selected to breastfeed found a striking six-fold increased infant mortality among infants that were fed breast milk substitutes. The excess mortality remained even when infants found to have HIV infection at one month of age were excluded from the analysis. Less than 4% of the households had access to tap water and most mothers did not follow guidelines for sterile preparation and storage of formula, cleansing of utensils, and avoidance of bottle feeds. Strategies for HIV-positive mothers such as prolonged infant prophylaxis or material antiretroviral treatment during lactation need closer consideration.


To date, an estimated 10% of children eligible for antiretroviral treatment receive it, and the frequency of retention in programmes is unknown. The authors evaluated the 2-year risks of death and loss to follow-up of children after antiretroviral treatment initiation in a
multicenter study in sub-Saharan Africa. Pooled analysis of routine individual data from 16 participating clinics produced overall Kaplan-Meier estimates of the probabilities of death or loss to follow-up after antiretroviral treatment initiation. Risk factors analysis used Weibull regression, accounting for between-cohort heterogeneity. The median age of 2405 children at antiretroviral treatment initiation was 4.9 years (12%, younger than 12 months), 52% were male, 70% had severe immunodeficiency, and 59% started antiretroviral treatment with a nonnucleoside reverse transcriptase inhibitor. The 2-year risk of death after antiretroviral treatment initiation was 6.9% (95% confidence interval [CI]: 5.9 to 8.1), independently associated with baseline severe anaemia (adjusted hazard ratio [aHR]: 4.10 [CI: 2.36 to 7.13]), immunodeficiency (adjusted aHR: 2.95 [CI: 1.49 to 5.82]), and severe clinical status (adjusted aHR: 3.64 [CI: 1.95 to 6.81]); the 2-year risk of loss to follow-up was 10.3% (CI: 8.9 to 11.9), higher in children with severe clinical status. The authors conclude that, once on treatment, the 2-year risk of death is low but the loss to follow-up risk is substantial. Antiretroviral treatment is still mainly initiated at advanced disease stage in African children, reinforcing the need for early HIV diagnosis, early initiation of antiretroviral treatment, and procedures to increase programme retention.

Editors' note: Although the 2-year risk of mortality after initiation of antiretroviral treatment was low, 75% of these deaths occurred in the first 6 months of treatment, with baseline HIV stage, nutritional status, and anaemia playing a role. The 10% programme attrition due to loss to follow-up constitutes a serious programme weakness that may reflect unreported death or moving; caregiver illness or death; inability to pay for transport, drugs, or laboratory tests; lack of follow-up procedures for no shows, or other causes. All programmes, whether adult or paediatric, should strive to minimize losses to follow-up by determining the causes and addressing them.

7. Structural determinants


It has been argued that women's economic vulnerability and dependence on men increases their vulnerability to HIV by constraining their ability to negotiate the conditions, including sexual abstinence, condom use and multiple partnerships, which shape their risk of infection. In the face of escalating infection rates among women, and particularly young women, many have pointed to the potential importance of economic empowerment strategies for HIV prevention responses. Global evidence suggests that the relationship between poverty and HIV risk is complex, and that poverty on its own cannot be viewed simplistically as a driver of the HIV epidemic. Rather, its role appears to be multidimensional and to interact with a range of other factors, including mobility, social and economic inequalities and social capital, which converge in a particularly potent way for young women living in southern Africa. To date, there have been few interventions that have explicitly attempted to combine economic empowerment with the goal of HIV prevention, and even fewer that have been rigorously evaluated. This paper explores how programmes such as microfinance, livelihood training and efforts to safeguard women's food security and access to property have begun to incorporate an HIV prevention focus. Although such circumscribed interventions, by themselves, are unlikely to lead to significant impacts on a national or regional scale, they are useful for testing cross-sectoral partnership models, generating practical lessons and providing a metaphor for what might be possible in promoting women's economic
empowerment more broadly. Despite numerous calls to ‘mainstream AIDS’ in economic development, cross-sectoral responses have not been widely taken up by government or other stakeholders. Kim and colleagues suggest potential reasons for limited progress to date and conclude by presenting programme and policy recommendations for further exploring and harnessing linkages between economic empowerment and HIV prevention in Southern Africa.

Editors’ note: This powerful article in a journal supplement of papers drawn from a UNAIDS-convened consultation on the vulnerability of young women in southern Africa uses the World Bank definition of empowerment: ‘the process of increasing the capacity of individuals or groups to make choices and to transform those choices into desired actions and outcomes’. It presents the evidence on microfinance, livelihood training, improving food security, and securing women’s property and inheritance rights, as well as recommendations for policy and programming on economic empowerment for HIV prevention. The entire supplement can be downloaded free of charge, if you are among the first 5000 people interested, at https://articleworks.cadmus.com/doc/926318


Kenya’s post-election violence in early 2008 created considerable problems for health services, and in particular, those providing HIV care. It was feared that the disruptions in services would lead to widespread treatment interruption. Medecins sans Frontieres had been working in the Kibera slum for 10 years and was providing antiretroviral therapy to almost 2000 patients when the violence broke out. Medecins sans Frontieres responded to the crisis in a number of ways and managed to keep HIV services going. Treatment interruption was less than expected, and Medecins sans Frontieres profited by a number of « lessons learned » that could be applied to similar contexts where a stable situation suddenly deteriorates.

Editors’ note: When an apparently stable situation deteriorates rapidly, clinic staff cannot get to work safely and patients cut off from health care services cannot access their medical records detailing their treatment regimens. Furthermore, acute trauma cases change workloads dramatically in clinics where the caseload is normally a mixture of primary health care problems and a comprehensive HIV programme. An updated Emergency Preparedness Plan, close communication ties with the community for daily situation assessments, emergency data management systems, and high levels of treatment literary motivating patients to seek creative solutions, can reduce the risk of antiretroviral treatment interruptions.

8. Food insecurity


The Academic Model Providing Access to Healthcare (AMPATH) is a partnership between Moi Teaching and Referral Hospital, Moi University School of Medicine, and a consortium of universities led by Indiana University. AMPATH has over 50000 patients in active care in 17 main clinics around western Kenya. Despite antiretroviral therapy, many patients were not
recovering their health because of food insecurity. AMPATH therefore established partnerships with the World Food Program and United States Agency for International Development and began high production farms to complement food support. Today, nutritionists assess all AMPATH patients and dependents for food security and refer those in need to the food program. Mamlin and colleagues describe the implementation, challenges, and successes of this program.

Editors’ note: This comprehensive programme combines HIV treatment initiation with extensive nutritional support for food-insecure patients (one-third) and their dependents for the 6 months needed to get them back to a productive life. Sustained through a combination of food production, food donation, and an effective food distribution infrastructure, including a computerized nutrition information system, this trailblazing programme aims to enhance income security for those patients who still need nutritional support after 6 months, rather than fostering dependency. They are referred to a family preservation initiative where they may benefit from, for example, microenterprise training, with or without microfinance, or participation in cooperatives with other patients to grow high value produce. It is time for domestic governments and international donors to step forward to replicate similar food security programmes for selected patients on antiretroviral treatment.


Participatory and interdisciplinary approaches have been suggested to develop appropriate agricultural innovations as an alternative strategy to improve food security and well-being among HIV affected households. However, sustainable implementation of such interactive approaches is far from easy and straightforward. This study reports of the Interactive Learning and Action approach, a methodology for agricultural innovation which has been adapted to the context of HIV. Role players in agriculture and health were brought together to stimulate and sustain innovation among three support groups for poor and affected households in a rural high HIV prevalence area in South Africa. The effectiveness of the approach was evaluated using both outcome and process criteria. The results indicate that an interactive approach in which service providers/researchers engage themselves as actors to explore the livelihood system and develop appropriate solutions in joint collaboration with resource users has potential. However, it also revealed that cooperation among participants and stakeholders at the interface of agriculture and HIV is complicated and sensitive to erosion. Of particular concern was the difficulty of mobilizing members from poor and affected households to participate and to overcome stigma and discrimination. Lessons and potential applications for the further development of interactive approaches are discussed.

Editors’ note: Interactive approaches build a close collaboration between relevant stakeholders to share knowledge, insights, experiences, needs, and creativity and to generate required involvement and ownership. The Interactive Learning Approach is characterised by enhancement of trust relationships, mutual learning, and knowledge integration between relevant stakeholders in a carefully guided process that is both interactive and iterative, around a shared vision. Adapting it to HIV clearly has some pitfalls, not the least of which are HIV illness and death, on the one hand, and stigma and discrimination on the other.
9. Treatment


Clinicians should be familiar with sex-specific considerations when managing antiretroviral treatment among women. Pregnancy is a critical influence on when to start treatment and what antiretroviral treatment should be included in a regimen. Sex, pregnancy and hormonal contraceptive therapies can each influence antiretroviral pharmacokinetic profiles. Women may be prone to have higher serum levels with selected antiretroviral treatments, which may improve potency but also increase the risk for toxicities. Several studies have demonstrated that women do have higher frequencies of selected antiretroviral-associated adverse events when compared with men. Although HIV treatment guidelines for nonpregnant women do not differ from men, clinicians should be aware of the high potential for certain antiretroviral-related toxicities and follow suggestions in order to decrease the risk of side effects.

Editors’ note: This summary of the literature and the US guidelines on antiretroviral treatment brings research gaps into sharp relief. Studies statistically powered to look at associations between age, HIV treatment, and outcomes by sex can help determine the trade-off for women between survival benefits and long-term toxicities. More study is needed of the safety of antiretroviral treatment discontinuation after pregnancy in women with higher CD4 cell counts, interactions between antiretroviral treatment and hormonal contraception, and the determinants of plasma-genital secretion viral load and viral sequence disconnects in women.


In 2008, 25 years after the human immunodeficiency virus (HIV) was discovered as the then tentative aetiological agent of acquired immune deficiency syndrome (AIDS), exactly 25 anti-HIV compounds have been formally approved for clinical use in the treatment of AIDS. These compounds fall into six categories: nucleoside reverse transcriptase inhibitors (NRTIs: zidovudine, didanosine, zalcitabine, stavudine, lamivudine, abacavir and emtricitabine); nucleotide reverse transcriptase inhibitors (NtRTIs: tenofovir); non-nucleoside reverse transcriptase inhibitors (NNRTIs: nevirapine, delavirdine, efavirenz and etravirine); protease inhibitors (PIs: saquinavir, ritonavir, indinavir, nelfinavir, amprenavir, lopinavir, atazanavir, fosamprenavir, tipranavir and darunavir); cell entry inhibitors (FIs: enfuvirtide) and co-receptor inhibitors (CRI: maraviroc); and integrase inhibitors (INIs: raltegravir). These compounds should be used in drug combination regimens to achieve the highest possible benefit, tolerability and compliance and to diminish the risk of resistance development.

Editors’ note: For readers who enjoyed biochemistry in the past or would like to learn more in the present, this article contains structural formulae, colourful 3-D depictions of docking by individual drugs, and clear descriptions of mechanisms of action by drug class. Those interested in history will find the dates of FDA approval for each drug, along with its manufacturer and generic and brand names, as well as a timeline showing the evolution of fixed-dose combinations.

This retrospective study identifies risk factors for mortality in a cohort of HIV-positive adult patients treated with highly active antiretroviral therapy in Jos, Nigeria. DeSilva and colleagues analyzed clinical data from a cohort of 1552 patients enrolled in an HIV treatment programme and started on antiretroviral treatment between December 2004 and 30 April 2006. Death was the study endpoint. Patients were followed in the study until death, being lost to follow-up, or the end of data collection, 1 December 2006. Baseline patient characteristics were compared using Wilcoxon Rank Sum Test for continuous variables and Pearson Chi-Square test for categorical variables to determine if certain demographic factors were associated with more rapid progression to death. The Cox proportional hazards multivariate model analysis was used to find risk factors. As of 1 December 2006, a total of 104 cases progressed to death. In addition to the expected association of CD4 count less than 50 at initiation of therapy and active tuberculosis with mortality, the patient characteristics independently associated with a more rapid progression to death after initiation of antiretroviral treatment were male gender, age less than 30 years old, and unemployment or unknown occupation status. Future research is needed to identify the confounding variables that may be amenable to targeted interventions aimed at ameliorating these health disparities.

Editors' note: In this retrospective cohort study of patients on antiretroviral treatment in one clinic, there was high loss to follow-up (8.8% over 23 months). Treatment adherence was not recorded for all patients and adequate nutrition was not measured, both of which are known to influence survival. However, the findings warrant further research, including qualitative studies, to assist in programme design to minimise loss to follow-up and prevent excessive mortality, particularly for young or unemployed men.

10. Comorbidities


Hessol and colleagues studied anal intraepithelial neoplasia and its associations with anal and cervical human papillomavirus (HPV), cervical neoplasia, host immune status, and demographic and behavioural risk factors in women with and at risk for HIV infection. They undertook a point-prevalence analysis nested within a prospective study of women seen at three clinical centres of the Women's Interagency HIV Study. In 2001-2003 participants were interviewed, received a gynaecological examination, anal and cervical cytology testing and, if abnormal, colposcopy-guided or anoscopy-guided biopsy of visible lesions. Exfoliated cervical and anal specimens were assessed for HPV using PCR and type-specific HPV probing. Logistic regression analyses were performed, and odds ratios (ORs) estimated risks for anal intraepithelial neoplasia. Four hundred and seventy HIV-infected and 185 HIV-uninfected women were enrolled. Low-grade anal intraepithelial neoplasia was present in 12% of HIV-infected and 5% of HIV-uninfected women. High-grade anal intraepithelial neoplasia was present in 9% of HIV-infected and 1% of HIV-uninfected women. In adjusted analyses among HIV-infected women, the risk factors for low-grade anal intraepithelial neoplasia were younger age [OR = 0.59, 95% confidence interval (CI) = 0.36-0.97], history of receptive
anal intercourse (OR = 3.2, 95% CI = 1.5-6.8), anal HPV (oncogenic types only OR = 11, 95% CI = 1.2-103; oncogenic and nononcogenic types OR = 11, 95% CI = 1.3-96), and cervical HPV (oncogenic and nononcogenic types OR = 3.5, 95% CI = 1.1-11). In multivariable analyses among HIV-infected women, the only significant risk factor for high-grade anal intraepithelial neoplasia was anal HPV infection (oncogenic and nononcogenic types OR = 7.6, 95% CI = 1.5-38). Even in the era of highly active antiviral therapy, the prevalence of anal intraepithelial neoplasia was 16% in HIV-infected women. After controlling for potential confounders, several risk factors for low-grade anal intraepithelial neoplasia differed from risk factors for high-grade anal intraepithelial neoplasia.

Editors’ note: In addition to these striking findings on low-grade and high-grade anal intraepithelial neoplasia in women with HIV infection, this study found an 80% prevalence of anal human papillomavirus (HPV) infection, exceeding the 45% prevalence of cervical HPV. Cervical HPV infection may serve as a reservoir and source of anal HPV infection or vice versa, with anal HPV infection possibly easier to detect. If these findings are corroborated, they may affect recommendations for screening for anal HPV infection and disease in HIV-positive women.

11. Reproductive health and HIV


Andia and colleagues investigated whether the prevalence of contraceptive use among women who are HIV-positive varied according to use of highly active antiretroviral therapy (HAART) in Mbarara, Uganda. They used data from a cross-sectional survey of 484 women who were HIV-positive (18-50 years) and were attending Mbarara University’s HIV clinic, 45% of whom were receiving HAART. Multivariate logistic regression was used to investigate the association between HAART use and contraceptive use. Data were collected between November 2005 and June 2006. Overall, 45% of the women were sexually active in the previous 3 months. Of these, 85% reported using contraceptive methods, with 84% reporting use of barrier contraceptive methods. Women receiving HAART were more than twice as likely to use contraceptive methods (adjusted odds ratio [AOR]=2.64; 95% confidence interval [CI]=1.07, 6.49) and more than 3 times as likely to use barrier contraceptive methods (AOR=3.62; 95% CI=1.54, 8.55) than were women not receiving HAART. The authors conclude that these findings support the need for increased attention to better integration of reproductive health and HIV services for women who are HIV positive.

Editors’ note: The Ugandan women on antiretroviral treatment in this study had been on treatment for a relatively short period (median 15 months) and 62% of them reported being sexually abstinent, possibly as a result of situational abstinence (30% of them were widows) rather than deliberate abstinence. Only 14% wanted more children but improved health status may increase fertility desires, a question that longer follow-up can help answer. In the meantime, this study underscores the importance of ensuring that antiretroviral treatment programmes offer women reproductive health care on site so that they can make informed choices and have the tools to act on them.

Antiretroviral therapy may influence the biological, social and behavioural determinants of pregnancy in HIV-infected women. However, there are limited longitudinal data on the reproductive intentions and outcomes among women on antiretroviral therapy in Africa. Using a prospective cohort design, Homsy and colleagues analyzed trends in desire for children and predictors of pregnancy among a cohort of 733 HIV-infected women in rural Uganda who initiated antiretroviral therapy between May 2003 and May 2004 and were followed up in their homes until June 2006. Women answered in-depth social and behavioural questionnaires administered every quarter in year 1 after initiating antiretroviral therapy, and every 6 to 12 months thereafter. Use of family planning methods was assessed at 18 and 24 months after starting antiretroviral therapy. The authors tested for non-constant pregnancy incidence by using a shape parameter test from the Weibull distribution. They modelled repeated measurements of all variables related to the women’s desire for children over time using a generalized estimating equation extension to the logistic regression model. Risk factors for pregnancy were examined using Cox proportional hazards model. 711 women eligible for the study were followed-up for a median time of 2.4 years after starting antiretroviral therapy. During this time, less than 7% of women reported wanting more children at any time point yet 120 (16.9%) women experienced 140 pregnancies and pregnancy incidence increased from 3.46 per 100 women-years in the first quarter to 9.5 per 100 women-years at 24 months (p<0.0001). This was paralleled by an increase in the proportion of women reporting sexual activity in the past 3 months, from 24.4% at baseline to 32.5% over 24 months of follow-up (p = 0.001). Only 14% of women used permanent or semi-permanent family planning methods by their second year on ART. In the multivariate model, younger age (HR = 2.71 per 10-year decrease, 95% CI: 2.95-3.78), having a body mass index>18.5 (HR = 1.09, CI:1.01-1.18) and not having used condoms consistently in the last 3 months (HR = 1.79, CI: 1.02-3.13) were independently associated with pregnancy. Women on antiretroviral therapy and their partners should be consistently counselled on the effects of antiretroviral therapy in restoring fertility, and offered regularly free and comprehensive family planning services as part of their standard package of care.

Editors’ note: Again from Uganda (see Andia et al abstract), this home-based AIDS care study documents the gap between not wanting more children and falling pregnant. The incidence of pregnancy increased over follow-up despite the fact that 93% of women repeatedly expressed not wanting or not planning to have more children. Following the study results, counsellors and nurses were retrained and then pro-actively counselled all registered clients on family planning quarterly, delivered hormonal contraceptives at home, and actively referred and followed up women opting for hormonal implants or tubal ligation. This is a good example of knowledge translation into action.

12. Sexual transmission

Moses and colleagues examined the impact of an intensive HIV preventive intervention among female sex workers on community HIV transmission, as represented by HIV prevalence among young antenatal clinic attenders in Karnataka state, south India. The preventive intervention was initiated in 18 of the 27 districts in Karnataka in 2003, and was generally at scale by mid-2005, covering over 80% of the urban female sex worker population. The authors examined trends over time in HIV prevalence from annual HIV surveillance conducted among antenatal clinic attenders in Karnataka under the age of 25 years from 2003 to 2007, comparing the preventive intervention with the other districts. Overall, HIV prevalence among antenatal clinic attenders under 25 years of age declined from 1.40% to 0.77%. In a multivariate model, the decline in HIV prevalence in the preventive intervention districts compared to the other districts was statistically significant (P = 0.01), with an adjusted annual odds ratio of 0.88 (95% CI 0.79-0.97). The decline in standardized HIV prevalence in the preventive intervention districts over the period was 56%, compared to 5% in the non-preventive intervention districts. Although this analysis is limited by lack of precise comparative data on intervention coverage and intensity, it supports the notion that scaled-up, intensive, targeted HIV preventive interventions among high-risk groups can have a measurable and relatively rapid impact on HIV transmission in the general population, particularly young sexually active populations as represented by antenatal clinic attenders. Such focused intervention programmes should be rapidly taken to scale in all HIV epidemics, and especially in concentrated epidemics such as in India.

Editors' note: This Avahan-supported programme of intensive prevention with female sex workers in 2500 sex work sites underscores the importance of programme scale reaching high coverage. Attributing HIV prevalence trend differentials in the general population on an ecological basis to specific activities or events in a sub-population is tenuous but, in the absence of other explanations, it does seem likely that one of the major reasons for the observed decline was the intensive prevention programmes led by both the governmental and non-governmental sectors in these districts.

13. Barrier protection


Beksinska and colleagues investigated how males assist their partners in using the female condom. A multi-site, randomized, cross-over trial was conducted to test the performance and acceptability of the Reality® female condom compared to a prototype similar in design and appearance but made of synthetic latex (FC2). In this study, women were asked about male partner assistance in female condom use. Partner assistance in female condom use was similar across female condom type. Of the women who returned for the first follow-up visit (n = 233), just over a third (35.2%) reported that the male partner assisted in the insertion compared to 26.4% of the 201 women who returned for the second visit. In most cases where the partner assisted, the device was inserted using the inner ring, as recommended in the instructions for use. A small number (6%) mentioned that partners assisted in removal. Men have a role to play in the use of the female condom and are willing to assist their partners in using it.

Editors' note: Most women in this study indicated that their partner liked the female condom and about a third reported partner assistance in its insertion and/or removal. Partners can check that the device is in place, ensure that it does not slip into the
vagina, and avoid entering to the side of the condom rather than inside it, known as 'misdirection' or 'penile misrouting'. Female condoms are rarely marketed to men and their participation is never emphasised in female condom promotion. It may be time to consider doing so, starting with discordant couple counselling.


The MIRA trial assessed whether providing diaphragm, lubricant gel, and condoms (intervention) compared with condoms alone (control) could reduce HIV incidence among 5,039 Southern African women. Compared with the control group, the cumulative proportion of last sex acts protected by any method was higher in the intervention group (OR \(= 1.33; 95\% CI\ 1.18, 1.49\)); however, only 36.3% of last sex acts were protected by both a male condom and a diaphragm, whereas 36.6% were protected by a diaphragm only. Product substitution (ever deciding to use a diaphragm instead of a condom in the previous 3 months) was reported at every visit by 22.4%, at some visits by 60.7%, and at none of the visits by 16.8% of these women. Women at greater risk for infection through their own or their partner's behaviour or who believed the diaphragm protected against HIV were more likely to report product substitution at every visit.

Editor's notes: In the MIRA (Methods for Improving Reproductive health in Africa) study, while the proportion of last sex acts protected was high (91.3% in the intervention group and 85.1% in the condom-only control group), only 53.5% of last sex acts were protected by a condom in the intervention group. For some women, 'prevention method optimism' appeared to have prevailed despite intensive counselling. For others, they may have been compelled to use a method of unknown efficacy instead of a proven but possibly less acceptable method (the male condom). Such product substitution would be understandable after a product has been proven to be effective but was frustrating for the research team trying to test the added benefit of the diaphragm over condom use alone.

14. Vaccines


Correlates of immune protection from HIV vaccines remain undefined. The first HIV vaccine efficacy trial in the US and Europe VAX004, was designed to assess whether rgp120 envelope subunits (AIDSVAX B/B, VaxGen) can induce partial or complete protection from HIV-1 infection. No effectiveness in the reduction of either the acquisition of infection or levels of plasma viraemia after HIV infection was noted. Jones and colleagues found evidence of vaccine-specific CD8+ T cells in volunteers who received the vaccine, regardless of behavioural risk. Surprisingly, the CD8-response is significantly higher in participants who would go on to contract HIV infection. These results suggest that AIDSVAX immunization may boost pre-existing immune responses due to pre-infection exposure, and a vaccine-induced immune profile may serve as a biological marker for HIV susceptibility.

Editors' note: It is not clear how the presence of a CD8+ T cell response, which is historically associated with the clearance of virus-infected cells, would be associated
with the risk of subsequent HIV infection. These results from the 2003 AIDS VAX trial come after those of the recent STEP vaccine study that suggested that vaccine-mediated T cell responses may have enhanced infection in uncircumcised vaccinees with prior immunity to adenoviruses. We are missing parts of the immunological puzzle. Vaccination before sexual debut would avoid pre-exposure to HIV but would it make a difference? Are genetic profiles conferring differential susceptibility? There is no dearth of questions in HIV vaccinology.

That was HIV this week, signing off.

Editors' notes on journal access:

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