Welcome to the 1st issue of HIV this month in 2014! In this issue, we cover the following topics:

1. **Reduce sexual transmission**
   - Large-scale partner notification of HIV is feasible in resource-poor settings
   - Time-space sampling can identify high-risk marginalised populations
   - Phylogenetic study shows that almost half of new infections among men who have sex with men occur in first year after infection
   - Low cost intervention package increases follow-up testing rates among couples attending voluntary HIV counselling and testing (VCT)
   - Renewed prevention efforts needed for key populations in Latin America and the Caribbean
   - Modeling study on generalized HIV epidemics demonstrates the importance of HIV transmission in both casual and stable partnerships

2. **Prevent HIV among drug users**
   - Female sex work in Central Asia: a neglected population for research and intervention

3. **Eliminate new HIV infections among children**
   - Outcomes up to 5 years among children exposed to zidovudine or nevirapine at birth
   - Safety of tenofovir during pregnancy

4. **15 million accessing treatment**
   - Progress in starting antiretroviral treatment earlier in Africa?
   - Pre-antiretroviral therapy losses to care: no time to lose

5. **Avoid TB deaths**
   - Response to measles vaccination in children on antiretroviral therapy

6. **Close the resource gap**
   - Gender, structural determinants and vulnerability

7. **Eliminate gender inequalities**
• Intimate partner violence as a barrier to condom and diaphragm use in southern Africa

8. Eliminate stigma and discrimination
• Stigma from health care professionals inhibits HIV testing among men who have sex with men in Viet Nam

9. Strengthening HIV integration
• Linking cervical cancer prevention into infrastructure for HIV services in sub-Saharan Africa
• Integrated paediatric services can improve uptake of HIV care but are still affected by stigma

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UNAIDS
1. Reduce sexual transmission

Scale-up and case-finding effectiveness of an HIV partner services program in Cameroon: an innovative HIV prevention intervention for developing countries.


Background: Partner services (PSs) are a long-standing component of HIV control programs in the United States and some parts of Europe. Small randomized trials suggest that HIV PS can be effective in identifying persons with undiagnosed HIV infection. However, the scalability and effectiveness of HIV PS in low-income countries are unknown.

Methods: We used data collected from 2009 to 2010 through a large HIV PS program in Cameroon to evaluate HIV PS in a developing country. HIV-positive index cases diagnosed in antenatal care, voluntary counseling and testing, and inpatient facilities were interviewed to collect information on their sexual partners. Partners were contacted via telephone or home visit to notify, test, and enroll those found to be HIV positive in medical care.

Results: Health advisors interviewed 1,462 persons with HIV infection during the evaluation period; these persons provided information about 1,607 sexual partners. Health advisors notified 1,347 (83.8%) of these partners, of whom 900 (66.8%) were HIV tested. Of partners tested, 451 (50.1%) were HIV positive, of whom 386 (85.6%) enrolled into HIV medical care. An average 3.2 index cases needed to be interviewed to identify 1 HIV case.

Conclusions: HIV PS can be successfully implemented in a developing country and is highly effective in identifying persons with HIV infection and linking them to care.

Editor’s notes: Partner notification of HIV status is a way to increase uptake of testing, and uptake of and adherence to antiretroviral therapy (ART) through mutual disclosure and support. However, partner disclosure is challenging and not commonly implemented in high prevalence settings. This paper reports on the first large-scale study in Africa of the effectiveness of HIV partner services in identifying persons with undiagnosed HIV infection. Health advisors asked HIV-index cases to identify partners in the past three years – the index cases were assured that all information collected would be kept confidential and their identities would not be revealed. Of the 1,607 partners reported by HIV-positive index cases, most (92%) were notified by health advisors rather than the index case. Over half (56%) received HIV testing through the partner services, of whom 50% tested HIV positive and 86% of the HIV positive partners were enrolled into care. There were no reported cases of domestic violence resulting from the partner services. These findings demonstrate that it is possible to provide HIV partner services to a large number of persons diagnosed with HIV infection at antenatal clinics, voluntary counselling and testing services (VCT) and inpatient health facilities in sub-Saharan Africa. Further studies on the potential social harms and benefits associated with partner services, cost-effectiveness, and risk behaviour are needed.

Sampling methodologies for epidemiologic surveillance of men who have sex with men and transgender women in Latin America: an empiric comparison of convenience sampling, time space sampling, and respondent driven sampling
Alternatives to convenience sampling (CS) are needed for HIV/STI surveillance of most-at-risk populations in Latin America. We compared CS, time space sampling (TSS), and respondent driven sampling (RDS) for recruitment of men who have sex with men (MSM) and transgender women (TW) in Lima, Peru. During concurrent 60-day periods from June-August, 2011, we recruited MSM/TW for epidemiologic surveillance using CS, TSS, and RDS. A total of 748 participants were recruited through CS, 233 through TSS, and 127 through RDS. The TSS sample included the largest proportion of TW (30.7 %) and the lowest percentage of subjects who had previously participated in HIV/STI research (14.9 %). The prevalence of newly diagnosed HIV infection, according to participants' self-reported previous HIV diagnosis, was highest among TSS recruits (17.9 %) compared with RDS (12.6 %) and CS (10.2 %). TSS identified diverse populations of MSM/TW with higher prevalences of HIV/STIs not accessed by other methods.

Abstract access

Editor's notes: This paper provides empirical data comparing three different strategies of epidemiological surveillance for men who have sex with men (MSM) and transgender women (TW) in Peru. All three samples identified a diverse sample of MSM/TW, with the time space sampling (TSS) method identifying the most diverse population with highest prevalence of HIV/STI. TSS is a location-based method that includes a preliminary ethnographic mapping process and randomly samples venue/date/time units which include a minimum number of potential participants. In this study, respondent driven sampling (RDS) performed less well, possibly due to the characteristics of seed participants, and geographical factors (urban sprawl), and a small number of recruitment waves. In contrast, TSS identified a large number of participants from previously undersampled populations – including the highest proportion of participants with undiagnosed HIV infection. It would be useful to conduct similar comparative studies in other settings.

HIV-1 transmission during early infection in men who have sex with men: a phylodynamic analysis.


Background: Conventional epidemiological surveillance of infectious diseases is focused on characterization of incident infections and estimation of the number of prevalent infections. Advances in methods for the analysis of the population-level genetic variation of viruses can potentially provide information about donors, not just recipients, of infection. Genetic sequences from many viruses are increasingly abundant, especially HIV, which is routinely sequenced for surveillance of drug resistance mutations. We conducted a phylodynamic analysis of HIV genetic sequence data and surveillance data from a US population of men who have sex with men (MSM) and estimated incidence and transmission rates by stage of infection.

Methods and findings: We analyzed 662 HIV-1 subtype B sequences collected between October 14, 2004, and February 24, 2012, from MSM in the Detroit metropolitan area, Michigan. These sequences were cross-referenced with a database of 30 200 patients diagnosed with HIV infection in the state of Michigan, which includes clinical information that is informative about the recency of infection at the time of diagnosis. These data were analyzed using recently developed population genetic methods that have enabled the estimation of transmission rates from the
population-level genetic diversity of the virus. We found that genetic data are highly informative about HIV donors in ways that standard surveillance data are not. Genetic data are especially informative about the stage of infection of donors at the point of transmission. We estimate that 44.7% (95% CI, 42.2%-46.4%) of transmissions occur during the first year of infection.

Conclusions: In this study, almost half of transmissions occurred within the first year of HIV infection in MSM. Our conclusions may be sensitive to un-modeled intra-host evolutionary dynamics, un-modeled sexual risk behavior, and uncertainty in the stage of infected hosts at the time of sampling. The intensity of transmission during early infection may have significance for public health interventions based on early treatment of newly diagnosed individuals.

Abstract Full-text [free] access

Editor’s notes: A better understanding of the intensity of transmission during different phases of infection is key to planning effective HIV prevention strategies. This study presents a novel approach using genetic sequence data from men who have sex with men (MSM) in Michigan. Viral load is high early after infection with HIV, before the immune system response begins. This paper estimates that during the first year of HIV infection, individuals are eight times as infectious as during chronic infection, and almost half of transmissions occur during the first year of infection. This underscores the importance of focusing on methods to increase earlier diagnosis, and partner notification approaches (see paper by Henley et al).

Predictors of first follow-up HIV testing for couples' voluntary HIV counseling and testing in Ndola, Zambia.


Introduction: We describe predictors of first follow-up testing for concordant negative and discordant couples seeking joint voluntary HIV counseling and testing in Ndola, Zambia, where cohabiting couples account for an estimated two-thirds of incident HIV infections.

Methods: Demographic and serostatus data were collected from couples' voluntary HIV testing and counseling (CVCT) and follow-up testing services implemented in government clinics. We calculated follow-up testing rates by serostatus and compared rates before and after the introduction of a Good Health Package (GHP).

Results: The follow-up testing rate from May 2011 to December 2012 was 12.2% for concordant negative (M-F-) couples and 24.5% for discordant (M+F- or M-F+) couples. Significant predictors of follow-up testing in multivariate analyses included increasing man's (aOR=1.02 per year) and woman's (aOR=1.02) age, the man being HIV+ (aOR=2.57), and the woman being HIV+ (aOR=1.89). The man (aOR=1.29) and the couple (aOR=1.22) having been previously tested for HIV were predictive of follow-up testing among discordant negative couples. Introduction of a GHP increased follow-up testing among discordant (aOR=2.93) and concordant negative (aOR=2.06) couples.

Conclusion: A low-cost GHP including prevention, screening, and treatment for common causes of morbidity and mortality resulted in increased follow-up testing rates among HIV discordant and concordant negative couples. Overall follow-up testing rates remain low and efforts to increase these rates are necessary in order to ensure linkage to combination prevention, reduce HIV transmission within couples and identify seroconversions promptly. Further investigation of low-cost sustainable incentives and other factors influencing follow-up HIV testing for couples is needed.
Abstract access

**Editor's notes:** Couples’ voluntary HIV counselling and testing (CVCT) offers a promising route for reaching high-risk individuals in sub-Saharan Africa, where heterosexual transmission predominates. Though found to be cost-effective in research settings, CVCT’s impact is limited by low rates of follow-up counselling. The investigators here analysed data from 10,806 couples attending CVCT services around Ndola, Zambia, of whom 12% were HIV-discordant couples and 88% were HIV-negative concordant. Follow-up visits were scheduled for three to eight weeks after the initial CVCT visit. Only 13.6% of couples attended this visit. The most substantial predictor for follow up for all couples was the presence of the Good Health Practice package of prevention, screening and treatment services at the clinic, which was associated with a doubling of the follow-up rate. These results provide further justification for integrating HIV services into primary health care services - and vice versa - and the benefits possible for multiple health conditions with this approach.

**Epidemiology of HIV in Latin America and the Caribbean.**

*De Boni R, Veloso VG, Grinsztejn B. Curr Opin HIV AIDS. 2014 Jan 3. [Epub ahead of print]*

Purpose of review: The aim of the present review is to update HIV/AIDS Epidemiology in Latin America and the Caribbean highlighting the concentrated aspect of epidemic in the region.

Recent findings: Among general population, HIV prevalence in Latin America is at stable levels (0.2-0.7%). The Caribbean still has one of the highest HIV prevalence rates in the world (<0.1-3%), but incidences have declined around 49%. This is not the current situation for high-risk key populations; most incident cases occur among MSM. Available data on transgender women suggest that they are the most-at-risk group. Female sex workers still have a 12-fold chance of being HIV positive compared with other women. IDU prevalence was revised to 0.45%, but non-IDU has been suggested as a mediator between sexual risk and HIV.

Summary: The increase in treatment coverage (mean is at 63%) resulted in modifications of HIV/AIDS epidemiology. New strategies to seek, test and link key populations to care are urgently needed and targeted interventions to prevent HIV expansion among them must be adopted. These strategies should consider the particular situation regarding social inequalities, discrimination and violence that pervade the HIV epidemic among key populations.

**Editor’s notes:** This review highlights recently published data on key populations in Latin America and the Caribbean, including men who have sex with men (MSM), transgender women, female sex workers and people who inject drugs. HIV remains a concentrated epidemic in Latin America and the Caribbean with MSM and transgender women being the most vulnerable populations. Although antiretroviral therapy (ART) coverage has increased to over 80% in several countries, a renewed focus on prevention, especially among key populations, is needed. It is estimated that prevention efforts currently only receive 15% of HIV public spending in this region. Culturally appropriate efforts are needed to identify and prevent HIV infection among key populations, and to better understand transmission dynamics of neglected groups such as transgender women.

HIV sexual transmission is predominantly driven by single individuals rather than discordant couples: a model-based approach.
Understanding the relative contribution to HIV transmission from different social groups is important for public-health policy. Information about the importance of stable serodiscordant couples (when one partner is infected but not the other) relative to contacts outside of stable partnerships in spreading disease can aid in designing and targeting interventions. However, the overall importance of within-couple transmission, and the determinants and correlates of this importance, are not well understood. Here, we explore how mechanistic factors - like partnership dynamics and rates of extra-couple transmission - affect various routes of transmission, using a compartmental model with parameters based on estimates from sub-Saharan Africa. Under our assumptions, when sampling model parameters within a realistic range, we find that infection of uncoupled individuals is usually the predominant route (median 0.62, 2.5%-97.5% quantiles: 0.26-0.88), while transmission within discordant couples is usually important, but rarely represents the majority of transmissions (median 0.33, 2.5%-97.5% quantiles: 0.10-0.67). We find a strong correlation between long-term HIV prevalence and the contact rate of uncoupled individuals, implying that this rate may be a key driver of HIV prevalence. For a given level of prevalence, we find a negative correlation between the proportion of discordant couples and the within-couple transmission rate, indicating that low discordance in a population may reflect a relatively high rate of within-couple transmission. Transmission within or outside couples and among uncoupled individuals are all likely to be important in sustaining heterosexual HIV transmission in sub-Saharan Africa. Hence, intervention policies should be broadly targeted when practical.

Abstract Full-text [free] access

Editor's notes: In 2008, Dunkle and colleagues argued that serodiscordant couples now contribute the majority of new HIV infections in generalized epidemics in sub-Saharan Africa (SSA). Ever since, the relative importance of discordant couples in the spread of HIV in generalized epidemics has been the subject of intense debate. Ultimately, this is a debate about resource allocation and revolves around the proposition that serodiscordant couples ought to be treated as a priority population for targeted HIV prevention.

In this study, a partnership-based compartmental model is used to compare the relative magnitude of transmissions within stable couples, transmission to and from uncoupled individuals, and extra-couple transmission to and from coupled individuals. The results lend support to other recent modelling work that suggests that all of these transmission routes are important to sustain heterosexual HIV epidemics in SSA (e.g., Bellan et al. 2013). Further, they argue that high levels of serodiscordance in the population are the result of past “non-couple routes of HIV transmission and their interactions with the partner switching dynamics”. High levels of serodiscordance, in turn, generate a potential for future transmissions within couples.

2. Prevent HIV among drug users

HIV among female sex workers in the Central Asian Republics, Afghanistan, and Mongolia: contexts and convergence with drug use.

Background: Central Asia is culturally and demographically diverse, both between and within its respective countries. That diversity is represented in the range of individual, network, community, and structural risks for female sex workers (FSWs) regionally. FSWs have several risk factors for HIV acquisition and transmission including behavioral, biological, and structural risk factors. Across Central Asia, sexual risks have become conflated with risks associated with injection and non-injection illicit drug use.

Methods: Peer-reviewed literature databases and gray literature were searched for articles on sex work in Central Asia. The medical subject heading (MeSH) of “sex work” was cross-referenced with terms associated with Uzbekistan, Tajikistan, Turkmenistan, Kazakhstan, Kyrgyzstan, Mongolia, and Afghanistan.

Results: HIV prevalence data for FSWs suggest sustained or increasing prevalence in the region. There are increasing data directly linking HIV among FSWs to injection drug use; odds of HIV are up to 20 times higher among FSWs reporting injecting drug use. Though injecting drug use among FSWs is rare in some settings, recreational drugs and alcohol use limits other risk reduction behaviors, such as condom use.

Conclusions: The Central Asian HIV epidemic has traditionally been assumed to be driven nearly exclusively by drug use, resulting in surveillance systems focused on parenteral transmission. The reviewed data highlight limited attention to characterizing the burden of HIV and risk factors for HIV acquisition and transmission among FSWs who use drugs. Moving forward will require enhanced HIV surveillance and research to inform HIV prevention approaches to address all levels of HIV risks affecting FSWs in Central Asia.

Abstract access

Editor’s notes: This paper summarises available data on HIV prevalence among female sex workers in Central Asia. The many gaps in information are striking – with data on HIV prevalence being available for only three of the seven countries reviewed, data on HIV among injecting female sex workers (FSW) available from three countries, and data on HIV among non-injecting female sex workers being available from one country only. The most detailed data came from Kyrgyzstan, where, as would be expected, injecting female sex workers were at greatest risk of HIV, and also had very high levels of hepatitis C infection. The findings highlight the need to expand surveillance systems in the region. Doing so will lead to better geographical coverage, and also to obtain more routinely compiled information on the extent of sex work and the prevalence of HIV infection among injecting and non-injecting sex workers. The high risk of HIV and hepatitis C infection among injecting FSW highlight also the importance of programmes for sex workers who inject drugs.

3. Eliminate new HIV infections among children


Objectives: To describe 5-year growth, survival, and long-term safety among children exposed to nevirapine or zidovudine in an African perinatal prevention trial, HIVNET 012.
Methods: All study children who were alive at the age 18 months were eligible for an extended follow-up study. Children whose families consented were enrolled and evaluated every 6 months from 24 to 60 months. At each visit, history, physical examination, and growth measures were taken. From these measurements, Z scores based on World Health Organization (WHO) standards were computed. Serious adverse event data were collected. Data from the initial and extended follow-up cohorts were included in the analysis.

Results: Five hundred twenty-eight study children were alive at the age 18 months and 491 (426 HIV uninfected and 65 infected) were enrolled into the follow-up study. Both exposed but uninfected children and HIV-infected children were substantially below WHO growth standards for weight and height. Head circumference Z scores for uninfected children were comparable with WHO norms. Five-year survival rates were 93% for uninfected children versus 43% for infected children. Long-term safety and growth outcomes in the 2 study arms were similar.

Conclusions: Both infected and uninfected children in the 5-year HIVNET 012 follow-up showed poor height and weight growth outcomes, underscoring the need for early nutritional interventions to improve long-term growth of all infants born to HIV-infected women in resource-limited settings. Similarly, the low 5-year survival among HIV-infected children supports the importance of early initiation of antiretroviral therapy. Both peripartum nevirapine and zidovudine were safe.

Abstract access

Editor’s notes: There are limited studies on outcomes in HIV exposed/negative and positive children beyond infancy in the pre-ART era in Africa. As expected, HIV positive children were twice as likely to die as HIV negative children. The five-year survival was significantly higher among children infected postnatally (after eight weeks) than among those infected perinatally. Notably, more than 50% of deaths among HIV positive children occurred in the first two years of life; HIV negative children who managed to survive to two years had a greater than 70% probability of survival to five years, irrespective of the timing of infection. Overall, poor growth (stunting and underweight) was common, but growth failure rates remained significantly higher in HIV positive children throughout the period of follow-up. Importantly, use of peripartum zidovudine or nevirapine did not result in any longterm adverse outcomes.

This study underscores the importance of early identification of HIV and timely institution of ART. However, a significant number of children do survive beyond infancy even without treatment, and therefore HIV testing strategies should also target older children who may have missed testing during infancy. Children in this setting remain highly vulnerable and growth monitoring and nutritional interventions are crucial. These should also be integrated within paediatric HIV care services.

Safety of tenofovir during pregnancy for the mother and fetus: a systematic review.


Tenofovir disoproxil fumarate (TDF) safety during pregnancy has important public health implications. This review summarizes TDF safety during pregnancy, focusing on pregnancy outcomes, congenital anomaly risk, and other potential toxicities on neonates. Although information is limited, TDF appears to be safe during pregnancy. In 6 studies of human immunodeficiency virus type 1 (and/or hepatitis B virus)-infected women receiving TDF during pregnancy, adverse events were mild to moderate; none were considered to be TDF-related. Five studies that followed in utero TDF-exposed infants showed no increased risk of growth or bone abnormalities. One study showed slightly
lower infant height at age 1 year, but the significance is unclear. The Antiretroviral Pregnancy Registry database, with 1,800 pregnancies exposed to TDF in the first trimester, does not indicate increased congenital anomaly risk with TDF exposure. More evidence collected prospectively, ideally with bone density measurements and randomized trial design, will be optimal to determine the effects of antenatal TDF exposure on children's health.

Abstract  Full-text [free] access

Editor's notes: Tenofovir is a well-tolerated antiretroviral drug which is effective against HIV and hepatitis B. Due to these favourable characteristics and its once-daily dosing, tenofovir is increasingly used in clinical practice. As a result, more women are exposed to this drug at conception and during pregnancy. Tenofovir is classified by the US Food and Drug Administration as a pregnancy category B drug. This means that there is insufficient evidence to determine risk in humans. The authors of this paper provide the reader with an updated systematic review of the safety of tenofovir in pregnancy. Amongst the studies looking at adverse events in infants and mothers, no serious adverse events occurred which were attributed to tenofovir. Likewise, no study identified an increased risk of growth or bone abnormalities in infants up to two years of age. These studies need to be interpreted with caution as many studies had small sample sizes and in some studies the duration of exposure to tenofovir was short (single dose-seven days). Arguably, the most reassuring evidence comes from the antiretroviral pregnancy registry database report, which showed no increased risk of congenital anomalies amongst 1,800 infants exposed to tenofovir in utero. This systematic literature review notes the paucity of available evidence to guide decision-making and highlights the need for further studies to determine the risk to humans of tenofovir exposure during pregnancy.

4. 15 million accessing treatment

Advanced HIV disease at entry into HIV care and initiation of antiretroviral therapy during 2006-2011: findings from four sub-Saharan African countries


Background: Timely antiretroviral therapy (ART) initiation requires early diagnosis of human immunodeficiency virus (HIV) infection with prompt enrollment and engagement in HIV care.

Methods: We examined programmatic data on 334,557 adults enrolling in HIV care, including 149,032 who initiated ART during 2006-2011 at 132 facilities in Kenya, Mozambique, Rwanda, and Tanzania. We examined trends in advanced HIV disease (CD4+ count <100 cells/µL or World Health Organization disease stage IV) and determinants of advanced HIV disease at ART initiation.

Results: Between 2006-2011, the median CD4+ count at ART initiation increased from 125 to 185 cells/µL an increase of 10 cells/year. Although the proportion of patients initiating ART with advanced HIV disease decreased from 42% to 29%, sex disparities widened. In 2011, the odds of advanced disease at ART initiation were higher among men (adjusted odds ratio [AOR], 1.4; 95% CI, 1.3-1.5), those on tuberculosis treatment (AOR, 1.6; 95% CI, 1.3-2.0), and those with a ≥12 month gap in pre-ART care (AOR, 2.0; 95% CI, 1.6-2.6).

Conclusions: Intensified efforts are needed to identify and link HIV-infected individuals to care earlier and to retain them in continuous pre-ART care to facilitate more timely ART initiation.

Abstract access

10
This large multi-cohort analysis of programmatic data from four sites in eastern and southern Africa shows slow but steady reductions in the proportions of patients starting antiretroviral treatment (ART) who have CD4 cell count <100 cells/µl, or WHO stage 4 disease. The risk of advanced disease at ART start was increased among men and among individuals with a long gap in pre-ART care, i.e. no clinic visit for a period of 12 or more months between enrolment and ART initiation. This study reiterates the need to strengthen strategies for retention and to reduce losses during the pre-ART cascade of care and the need to focus interventions on men.

Adults receiving HIV care before the start of antiretroviral therapy in sub-Saharan Africa: patient outcomes and associated risk factors.


Background: Gaining understanding of the period before antiretroviral therapy (ART) is needed to improve treatment outcomes and to reduce HIV transmission. This study describes the cascade of enrollment in HIV care, pre-ART follow-up, and predictors of mortality and lost to follow-up (LTFU) before ART initiation.

Methods: We conducted a cohort study among HIV-infected adult patients not yet started on ART in 4 HIV sub-Saharan African programs. Patient follow-up began at enrollment and ended at the earliest of death, transfer-out, ART initiation, last visit date, or 60 months postenrollment. Risk factors for death and LTFU were investigated during the periods 0-6 and 6-60 months.

Results: A total of 55,789 patients (65.4% women) were included as follows: 44.2% in clinical stage 3 or 4, with median CD4 of 261 cells per microliter [interquartile range (IQR): 125-447]. Patient care started with a median of 3 days (IQR: 0-11) after HIV diagnosis, and 31,104 of 55,789 (55.8%) patients had CD4 counts performed within 1 month of enrollment. Of 47,283 patients with known ART eligibility status at enrollment, 36,969 (78.2%) patients required ART and 27,798 of 36,969 (75.7%) patients initiated therapy. Median follow-up was 2.5 months (IQR: 0.9-13.1). Mortality and LTFU rates were 3.9 per 100 person-years [95% confidence interval (CI): 3.7 to 4.1] and 28.3 per 100 person-years (95% CI: 27.8 to 28.8), respectively. Regardless of period, increased mortality and LTFU were associated with male, lower body mass index, advanced clinical stage, and lower CD4 cell count.

Conclusions: Short delays between HIV testing and care enrollment were observed in our HIV programs, but delays to determine ART eligibility were long. Interventions to initiate ART earlier, specifically targeted to men, are needed to improve patient retention in Africa.

Abstract access

Editor’s notes: This large study from four sites in east Africa confirms the findings of other studies from sub-Saharan Africa which have documented substantial losses to care among patients during the care cascade, between the time of HIV testing and starting antiretroviral treatment (ART). The proportion of patients lost to follow-up was particularly striking and the strong association with disease stage suggests that this group may include many unascertained deaths. The need to strengthen and expedite each step of the care cascade is clear.

5. Avoid TB deaths
Changes in measles serostatus among HIV-infected Zambian children initiating antiretroviral therapy before and after the 2010 measles outbreak and supplemental immunization activities.


Background: In 2010, Zambia had a large measles outbreak, providing an opportunity to measure changes in measles serostatus following highly active antiretroviral therapy (HAART), exposure to measles virus, and revaccination among children infected with human immunodeficiency virus (HIV).

Methods: A prospective cohort study of 169 HIV-infected Zambian children aged 9-60 months with a history of measles vaccination was conducted to characterize the effects of HAART and revaccination on measles immunoglobulin G (IgG) serostatus by enzyme immunoassay.

Results: Prior to the measles outbreak, only 23% of HIV-infected children were measles IgG seropositive at HAART initiation. After adjusting for 6-month changes in baseline age and 5% changes in nadir CD4+ T-cell percentage, HAART was not associated with measles IgG seroconversion. However, 18 of 19 children seroconverted after revaccination. Eight children seroconverted during the outbreak without revaccination and were likely exposed to wild-type measles virus, but none were reported to have had clinical measles.

Conclusions: Immune reconstitution after HAART initiation did not restore protective levels of measles IgG antibodies, but almost all children developed protective antibody levels after revaccination. Some previously vaccinated HIV-infected children had serological evidence of exposure to wild-type measles virus without a reported history of measles.

Abstract access

Editor’s notes: Successful immunisation campaigns in Africa resulted in >90% decline in measles cases by 2008. However, maintenance of high levels of population immunity and surveillance are vital to prevent outbreaks. HIV-positive children have lower response rates to measles vaccination and a poorer qualitative response to the vaccine compared to HIV-negative children. This study showed that less than 50% of vaccinated HIV-positive children had protective antibody levels. Immune reconstitution after starting antiretroviral therapy (ART) did not have any effect to restore protective antibody levels to measles virus. But, revaccination did result in most children seroconverting (i.e. developing protective measles antibodies).

With the scale up of ART, HIV-associated mortality has declined substantially. However, immune reconstitution does not restore protection against these infections. Further, the increased survival due to ART also results in an accumulation of HIV-positive children susceptible to diseases such as measles. The findings of this study would support revaccination of HIV-positive children not only for individual protection but also for measles elimination.

6. Close the resource gap

A critical analysis of Peru’s HIV grant proposals to the Global Fund.

Peru has applied to six of the Global Fund to Fight AIDS, Tuberculosis and Malaria (the Global Fund) rounds for funding, achieving success on four occasions. The process of proposal development has, however, been criticised, especially concerning the use of evidence, relevance/consistency and performance indicators. We aimed to analyse the Peruvian Global Fund proposals according to those dimensions, providing feedback to improve future local efforts and inform global discussions around Global Fund procedures. We analysed the content of four HIV-focused proposals (rounds 2, 5, 6 and 8) regarding epidemic context, needs identification and prioritisation and monitoring and evaluation systems. Peruvian proposals submitted after round 1 were described as resulting from collaborative inputs involving formerly unrepresented sectors, principally 'vulnerable populations'. However, difficulties arose regarding the amount and quality of evidence about the epidemiological context; limited consideration of social determinants of the epidemic; lack of theory-driven interventions, and little synergy across projects and the inclusion of weak monitoring and evaluation systems, with poor indicators and measurement procedures. Prioritising the development of analytical and technical skills to generate Global Fund proposals would enhance the country's capacity to produce and utilise evidence, improve the technical-political interface, strengthen information systems and lead to more informed decision making and accountability.

Abstract access

Editor’s notes: This is a useful paper that dissects one country’s Global Fund proposals over 10 years (2002-2012) to assess the use of evidence, the consistency and appropriateness of proposed activities and the adequacy of its monitoring and evaluation framework. Although only one country, Peru, is scrutinised in this paper, many of the findings will be relevant to the development and implementation of Global Fund proposals in other countries.

It was encouraging to learn that the use of evidence improved over time. However the lack of appropriate surveillance data meant that proposals were not always found to be evidence-based. The paper highlights in particular the need to use epidemiological evidence that is related to specific population sub-categories to address “vulnerability” and ensure that interventions are effectively targeted.

Consistency and continuity across proposals was sometimes lacking, possibly reflecting the Global Fund’s mechanistic funding process via “rounds”. The paper notes that at times, programmes could appear to be a juxtaposition of activities rather than a well thought out comprehensive strategy. It would be interesting to see whether the Global Fund's new funding model based on the national HIV/AIDS strategy in the future leads to a more continuous and consistent flow of activities.

Another key point in the paper is the inadequacy of the proposals’ monitoring and evaluation (M&E) framework to monitor grants and evaluate results. As the paper notes, the information system will need to be strengthened for the M&E to deliver a more evidence based strategy.

7. Eliminate gender inequalities

Intimate partner violence and condom and diaphragm non-adherence among women in an HIV prevention trial in southern Africa.

Background: We **longitudinally examined the effect of intimate partner violence (IPV) on condom and diaphragm non-adherence among women** in the Methods for Improving Reproductive Health in Africa study, a phase III HIV prevention trial in southern Africa.

Methods: **Recent IPV** (fear of violence, emotional abuse, physical violence, or forced sex, in past 3 months), condom nonadherence, and diaphragm nonadherence were assessed at baseline, 12 month, and exit visits (up to 24 months). The association between IPV and (1) condom nonadherence or (2) diaphragm nonadherence across visits was modeled using Generalized Estimating Equations adjusting for potential confounders.

Results: Of 4,505 participants, **55% reported recent IPV** during their trial participation. Women reported **fearing violence** (41%), emotional abuse (38%), being physically assaulted (16%), and **forced sex** (15%) by their regular male partner. IPV was associated with condom nonadherence in both study arms [adjusted odds ratio (AOR): 1.41, 95% confidence interval (CI): 1.24 to 1.61 (control arm) and AOR: 1.47, 95% CI: 1.28 to 1.69, (intervention arm)] **and with diaphragm nonadherence** (AOR 1.24, 95% CI: 1.06 to 1.45) adjusting for age, study sites, number of sex partners, and knowledge of male partner infidelity. Modeling effects of each form of IPV separately on nonadherence outcomes yielded similar results.

Conclusions: Prevalence of recent IPV was high and associated with condom and diaphragm nonadherence during the trial. **Counseling in prevention trials should proactively address IPV**, for its own sake, and in product and risk-reduction counselling. Strategies to encourage men's positive involvement in product use and prevent IPV perpetration should be considered.

Abstract access

**Editor’s notes:** There is growing recognition that gender inequality and violence are important structural drivers of HIV vulnerability among women. This is one of a small number of longitudinal studies exploring this relationship, with the findings complementing other longitudinal evidence from South Africa and Uganda. Evidence shows that exposures to intimate partner violence are associated with incident HIV infection. The study utilized a relatively short recall period of the past three months. Despite this, it illustrates high levels of partner violence that participants experienced, and its significant association with inconsistent condom and diaphragm use. Interestingly, these associations did not appear to differ substantially by the form of partner violence experienced. This suggests that it is not only physical or sexual violence that is important. The authors stress the need to proactively integrate counselling on intimate partner violence into prevention trials. More broadly, the findings suggest that additional programme components may be needed, to enable women in violent relationships to benefit from HIV prevention technologies.

8. Eliminate stigma and discrimination

‘Never testing for HIV’ among men who have sex with men in Viet Nam: results from an internet-based cross-sectional survey.

Background: Men who have sex with men in Viet Nam have been under-studied as a high-risk group for HIV infection, and this population's percentage and determinants of HIV testing have not been comprehensively investigated.

Methods: A national Internet-based survey of self-reported sexual and health seeking behaviours was conducted between August and October 2011 with 2 077 Vietnamese men who had sex with men in the last twelve months to identify the frequency of 'never testing for HIV' among Internet-using MSM living in Viet Nam, as well as the factors associated with this HIV-related high-risk behavior. Logistic regression analyses were conducted to assess the demographic characteristics and behaviours predicting never testing for HIV.

Results: A total of 76.5% of men who have sex with men who were surveyed reported never having been voluntarily tested for HIV. Predictors of never being tested included having a monthly income less than VND 5 Million, being a student, using the Internet less than 15 hour per week, and not participating in a behavioural HIV intervention.

Conclusions: Never testing for HIV is common among Internet-using men who have sex with men in Viet Nam. Given the dangerously high prevalence of this high-risk behaviour, our findings underscore the urgent need for segmented and targeted HIV prevention, care and treatment strategies, focusing on drastically reducing the number of men who have sex with men never testing for HIV in Viet Nam.

Abstract  Full-text [free] access

Editor’s notes: There is growing concern about new and resurging epidemics among men who have sex with men (MSM) globally. Previous data from Viet Nam have estimated HIV prevalence of around 20%. The low rate of HIV-testing found in this fairly large study of men who reported having sex with men in the past 12 months, is therefore quite alarming. The most common reasons for not having tested were an assumption of being HIV-negative, stigma (from health professionals), fear associated with testing and lack of knowledge about where to go to be tested. This study highlights the critical gaps in HIV testing in this setting and the urgent need to focus sexual health resources on the provision of sexual health services for MSM free from stigma and discrimination. The study also highlights the need for increasing awareness of the availability and importance of HIV testing among sexually active MSM.

9. Strengthening HIV integration

Infrastructure requirements for human papillomavirus vaccination and cervical cancer screening in sub-Saharan Africa.


The availability of both human papillomavirus (HPV) vaccination and alternative screening tests has greatly improved the prospects of cervical cancer prevention in sub-Saharan African (SSA) countries. The inclusion of HPV vaccine in the portfolio of new vaccines offered by the Global Alliance for Vaccines and Immunization (GAVI) to GAVI-eligible countries has vastly improved the chances of introducing HPV vaccination. Further investments to improve vaccine storage, distribution and delivery infrastructure and human resources of the Extended Programme of Immunization will substantially contribute to the faster introduction of HPV vaccination in SSA countries through both school- and campaign-based approaches. Alternative methods to cytology for
the prevention of cervical cancer through the early detection and treatment of cervical cancer precursors have been extensively evaluated in the past 15 years, in Africa as well as in other low-resource settings. Visual inspection with 3-5% dilute acetic acid (VIA) and HPV testing are the two alternative screening methods that have been most studied, in both cross-sectional and randomised clinical trials. VIA is particularly suitable to low-resource settings; however, its efficacy in reducing cervical cancer is likely to be significantly lower than HPV testing. The introduction of VIA screening programmes will help develop the infrastructure that will, in turn, facilitate the introduction of affordable HPV testing in future. Links with the existing HIV/AIDS control programmes is another strategy to improve the infrastructure and screening services in SSA. Infrastructure requirements for an integrated approach aiming to vaccinate single-year cohorts of girls in the 9-13 years age-range and to screen women over 30 years of age using VIA or affordable rapid HPV tests are outlined in this manuscript.

Abstract access

Editor’s notes: Infection with human papillomavirus (HPV) can lead to cervical cancer. HIV-positive women are more likely to acquire and have persistent HPV, so the high burden of HIV in sub-Saharan Africa (SSA) contributes to the burden of cervical cancer. This review article discusses the options for the prevention of cervical cancer in SSA. While this article is primarily focused on cervical cancer, it highlights the potential linkages of prevention activities with HIV/AIDS services with an emphasis on infrastructure to improve access to these services for women in SSA. The options for cervical cancer prevention in SSA include HPV vaccination, visual inspection tests, HPV DNA tests and cytology screening. These options and the infrastructure required for each are described in detail, and some of the barriers to delivery are highlighted. Treatment options are also described, including cryotherapy following visual inspection.

Qualitative assessment of the integration of HIV services with infant routine immunization visits in Tanzania.


Background: In 2009, a project was implemented in 8 primary health clinics throughout Tanzania to explore the feasibility of integrating pediatric HIV prevention services with routine infant immunization visits.

Methods: We conducted interviews with 66 conveniently sampled mothers of infants who had received integrated HIV and immunization services and 16 providers who delivered the integrated services to qualitatively identify benefits and challenges of the intervention midway through project implementation.

Findings: Mothers' perceived benefits of the integrated services included time savings, opportunity to learn their child’s HIV status and receive HIV treatment if necessary. Providers’ perceived benefits included reaching mothers who usually would not come for only HIV testing. Mothers and providers reported similar challenges, including mothers' fear of HIV testing, poor spousal support, perceived mandatory HIV testing, poor patient flow affecting confidentiality of service delivery, heavier provider workloads, and community stigma against HIV-infected persons; the latter a more frequent theme in rural compared to urban locations.

Interpretation: Future scale-up should ensure privacy of these integrated services received at clinics and community outreach to address stigma and perceived mandatory testing. Increasing human
resources for health to address higher workloads and longer waiting times for proper patient flow is necessary in the long term.

Abstract access

**Editor's notes:** In response to the poor uptake of antiretroviral therapy (ART) by children in Tanzania the Tanzanian Ministry of Health and Social Welfare and the US Centres for Disease Control and Prevention implemented a project to integrate early infant HIV diagnosis (EID) into routine immunisation visits in four urban and four rural clinics. The authors conducted a qualitative study to explore perceptions of this integrated service by mothers and health care providers. They conducted a large number of in depth interviews with mothers (66) and with health care providers (16). The majority of mothers and providers perceived the integrated services to be beneficial in relation to improving the uptake of HIV care and treatment. This is especially so as existing trust in immunisation services ensured that women were attending these services. However, they found a number of mixed messages about benefits for the mothers in terms of reduced costs and time in accessing both services together. Whilst most women reported cost and time savings, other women and providers reported that women spent a long time at the clinic, especially when queuing for both services. There were also issues in relation to confidentiality at the clinics concerning HIV status. Whilst many women trusted the staff to keep their information confidential, there were a number of ways in which the clinic processes were seen to compromise confidentiality. These included providing HIV services to groups of mothers together or providing care in designated HIV treatment rooms, which could be identified by other women at the clinic. This concern with confidentiality was important as women reported issues about stigma within their communities and fear of disclosure to partners or husbands who may be violent or leave them. There are concerns that this may impact on the uptake of immunization and the authors reported evidence of this in the rural clinics, from quantitative studies. This paper highlights that future planning to provide more efficient services and increased uptake of HIV care and treatment needs to be highly sensitive to the ongoing issue of disclosure and stigma. Integrated services may provide a way to address this by providing all the services (such as immunisation and HIV care) in one session. In this way, other patients or mothers are not aware who is receiving HIV care. As the authors note though, this has implications for resource allocation.