Welcome to **HIV this month**! In this issue, we cover the following topics:

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UNAIDS
1. **Reduce sexual transmission**

Multiple sexual partnerships among female adolescents in rural Uganda: the effects of family structure and school attendance.


**Background:** A better understanding is needed of the contextual factors that influence HIV risk behaviors among female adolescents in sub-Saharan Africa. The objectives of this study were to assess the influence of family structure on lifetime sexual partners and on the number of sexual partners in the last year among female adolescents in rural Rakai, Uganda. In addition, the study assessed whether the influence of family structure on these outcomes differed by the school attendance status of the adolescents.

**Methods:** The sample consisted of 2337 unmarried adolescent girls, aged 15-19, enrolled in the Rakai Community Cohort Study. The last survey interview within the time period of 2001-2008 available for each girl was used. Analyses were stratified by age (15-17 year olds and 18-19 year olds) and school status. Multinomial logistic and poisson regressions were used.

**Results:** Living in a household with a biological father was protective against both outcomes. Family structure was not associated with the outcomes among in-school adolescents but it was significantly associated with the outcomes among out-of-school adolescents.

**Conclusions:** The findings suggest that understanding the familial context in which female adolescents develop, as well as its interaction with school attendance, is important for HIV prevention efforts. Both research and programmatic initiatives must consider the interplay between the family and school domains when considering ways to reduce HIV acquisition among adolescent women.

**Editor’s notes:** This study addresses the key issue of adolescent sexual behaviour among unmarried girls which itself has significant implications for HIV and other STI risk. Only about 40% of girls in this study lived in a family structure which included a biological father in the household. Living with their own father was protective against having multiple partners. The authors highlight that cultural factors may lead to reverse causality behind this finding – including the fact that girls who got pregnant were made to leave the parental home. However, the biological father’s role in protecting daughters from sexual advances and exploitation is also suggested as an underlying reason. A novel finding of this study was the fact that family structure influenced sexual behaviour of non-school going girls but did not influence school-going girls. It is unclear whether school-attendance was itself protective or whether girls who went to school came from more supportive backgrounds in the first place. The authors emphasise that more research is needed to understand the pathways underlying this finding.

**Countries:** Uganda

**Region:** Africa

**Sub-categories:** gender, structural determinants and vulnerability
Traumatic stress and the mediating role of alcohol use on HIV-related sexual risk behavior: Results from a longitudinal cohort of South African women who attend alcohol-serving venues.


Background: In South Africa, alcohol contributes to the HIV epidemic, in part, by influencing sexual behaviors. For some, high levels of alcohol consumption may be driven by previous traumatic experiences that result in traumatic stress. The purpose of this study was to quantify the longitudinal association between traumatic stress and unprotected sex among women who attend drinking venues and to assess whether this association was explained by mediation through alcohol use.

Methods: Data were collected in four waves over a year from a prospective cohort of 560 women who regularly attended alcohol-serving venues in a Cape Town township. Longitudinal mixed models examined: 1) the relationship between traumatic stress and counts of unprotected sex, and 2) whether alcohol use mediated the association between traumatic stress and unprotected sex.

Results: Most women reported elevated traumatic stress (80%) and hazardous alcohol use (88%) at least once during the study period. In models adjusted for covariates, traumatic stress was associated with unprotected sex (b=0.28, SE=0.06, t=4.82, p<.001). In addition, traumatic stress was associated with alcohol use (b=0.27, SE=0.02, t=14.25, p<.001), and was also associated with unprotected sex (b=0.20, SE=0.06, t=3.27, p<.01) while controlling for alcohol use (b=0.28, SE=0.07, t=4.25, p<.001). The test for the mediated effect established that alcohol use was a significant mediator, accounting for 27% of the total effect of traumatic stress on unprotected sex.

Conclusions: These results highlight the need to address traumatic stress among female venue patrons as an important precursor of HIV risk due to alcohol use.

Abstract access

Editor’s notes: There is an established link between alcohol use and high-risk sexual behaviour, but the role of mental health in this relationship is often overlooked. Traumatic stress can lead to problematic drinking patterns and increased high-risk sexual behaviour. These negative coping mechanisms may in turn increase traumatic stress, further elevating the risk of HIV infection. A longitudinal cohort study of 560 South African women was conducted to quantify this association. The study benefits from a large sample size and good participant retention throughout the study period.

Traumatic stress was measured using a 17-item Post Traumatic Stress Disorder checklist (PCL) and alcohol use was measured using the 10-item Alcohol Use Disorders Identification Test (AUDIT). The primary outcome was the number of unprotected sexual events that participants reported having in the previous four months. Participants who scored higher for traumatic stress and alcohol use reported having more unprotected sex. Traumatic stress was also found to be independently associated with alcohol use. These findings provide support for programmes that focus on both alcohol use and traumatic stress, owing to their tendency to co-occur and heighten the risk of HIV infection. The authors recommend adapting such programmes to the South African setting and call for further research into how best to identify women at risk of traumatic stress in South African drinking venues.

Countries: South Africa
Region: Africa
Combination HIV prevention among MSM in South Africa: results from agent-based modeling.


HIV prevention trials have demonstrated the effectiveness of a number of behavioral and biomedical interventions. **HIV prevention packages are combinations of interventions and offer potential to significantly increase the effectiveness of any single intervention.** Estimates of the effectiveness of prevention packages are important for guiding the development of prevention strategies and for characterizing effect sizes before embarking on large scale trials. Unfortunately, most research to date has focused on testing single interventions rather than HIV prevention packages. Here we report the results from agent-based modeling of the effectiveness of HIV prevention packages for men who have sex with men (MSM) in South Africa. We consider packages consisting of four components: antiretroviral therapy for HIV infected persons with CD4 count <350; PrEP for high risk uninfected persons; behavioral interventions to reduce rates of unprotected anal intercourse (UAI); and campaigns to increase HIV testing. We considered 163 HIV prevention packages corresponding to different intensity levels of the four components. We performed 2252 simulation runs of our agent-based model to evaluate those packages. **We found that a four component package consisting of a 15% reduction in the rate of UAI, 50% PrEP coverage of high risk uninfected persons, 50% reduction in persons who never test for HIV, and 50% ART coverage over and above persons already receiving ART at baseline, could prevent 33.9% of infections over 5 years (95% confidence interval, 31.5, 36.3).** The package components with the largest incremental prevention effects were UAI reduction and PrEP coverage. The impact of increased HIV testing was magnified in the presence of PrEP. **We find that HIV prevention packages that include both behavioral and biomedical components can in combination prevent significant numbers of infections with levels of coverage, acceptance and adherence that are potentially achievable among MSM in South Africa.**

**Editor's notes:** The HIV epidemic among men who have sex with men (MSM) in sub-Saharan Africa continues to grow and focused prevention efforts are needed for this population. This is one the first studies to model the effectiveness of a combination HIV prevention study among MSM, and one of few modelling studies among MSM in Africa. This paper finds that a potentially achievable combination package of increased HIV testing, condom use, PrEP and antiretroviral therapy could prevent about a third of new infections over the next five years. The component with the largest incremental impact on infections was the behavioural component. This resulted in a 15% reduction in unprotected anal intercourse. **This finding emphasises the need for renewed efforts to reinforce behavioural approaches to HIV prevention,** which also have lower resource requirements than the biomedical components included in these models. **Further work on understanding associations with regard to uptake and adherence to programmes among MSM in sub-Saharan Africa would be very useful to help design focused programme packages.**

**Countries:** South Africa  
**Region:** Africa
2. Prevent HIV among drug users

HIV prevalence and risk behaviors among people who inject drugs in two serial cross-sectional respondent-driven sampling surveys, Zanzibar 2007 and 2012


People who inject drugs (PWID) are at higher risk of acquiring HIV due to risky injection and sexual practices. We measured HIV prevalence and behaviors related to acquisition and transmission risk at two time points (2007 and 2012) in Zanzibar, Tanzania. We conducted two rounds of behavioral and biological surveillance among PWID using respondent-driven sampling, recruiting 499 and 408 PWID, respectively. Through face-to-face interviews, we collected information on demographics as well as sexual and injection practices. We obtained blood samples for biological testing. We analysed data using RDSAT and exported weights into STATA for multivariate analysis. HIV prevalence among sampled PWID in Zanzibar was 16.0% in 2007 and 11.3% in 2012; 73.2% had injected drugs for 7 years or more in 2007, while in the 2012 sample this proportion was 36.9%. In 2007, 53.6% reported having shared a needle in the past month, while in the 2012 sample, 29.1% reported having done so. While 13.3% of PWID in 2007 reported having been tested for HIV infection and received results in the past year, this proportion was 38.0% in 2012. Duration of injection drug use for 5 years or more was associated with higher odds of HIV infection in both samples. HIV prevalence and indicators of risk and preventive behaviors among PWID in Zanzibar were generally more favorable in 2012 compared to 2007—a period marked by the scale-up of prevention programs focusing on PWID. While encouraging, causal interpretation needs to be cautious and consider possible sample differences in these two cross-sectional surveys. HIV prevalence and related risk behaviors persist at levels warranting sustained and enhanced efforts of primary prevention and harm reduction.

Abstract access

Editor’s notes: People who inject drugs (PWID) are a marginalized or key population in Africa, and throughout the world. They suffer from disproportionately high rates of HIV infection and other diseases. Like other key populations such as sex workers, the criminalization of PWID makes it difficult to provide specialized services. Members of this community are often fearful of programmes which might identify them. This dynamic causes viruses such as HIV to go undetected and unmanaged. This is evidenced by the difference in HIV prevalence through this study in Zanzibar, United Republic of Tanzania between the general population at 1% and the rates in PWID at 16.0% and 11.3% in 2007 and 2012 respectively. Although the study highlighted where HIV prevalence might be reducing and behaviours such as HIV testing might be improving, multi-person use of contaminated injecting equipment went slightly up. These data are confounded by the fact that it is unclear whether the same segment of the population was surveyed, and by the fact that so few females participated. Issues with recruitment shed light on how difficult it can be to reach these communities. This can usually be attributed to criminalization and distrust, but also to mobility and the lack of engagement generally of governments and local health programmes in acknowledging the need to address and support the specialized needs of PWID communities. To date, there has been little recognition of injection drug use in Africa and the related health needs of these communities,
which can vary depending on context and country. Studies such as this one, even with the limitations of recruitment and comparability of samples, should be undertaken more often and with in-depth qualitative components, as mentioned by the authors, to further explore how these communities might be accessed and their needs addressed.

**Countries:** United Republic of Tanzania  
**Region:** Africa  
**Sub-categories:** Injecting drug use, HIV prevention

### 3. Eliminate new HIV infections among children

**Morbidity in relation to feeding mode in African HIV-exposed, uninfected infants during the first 6 mo of life: the Kesho Bora study.**


**Background:** Refraining from breastfeeding to prevent HIV transmission has been associated with increased morbidity and mortality in HIV-exposed African infants.

**Objective:** *The objective was to assess risks of common and serious infectious morbidity by feeding mode in HIV-exposed, uninfected infants ≤6 mo of age* with special attention to the issue of reverse causality.

**Design:** HIV-infected pregnant women from 5 sites in Burkina Faso, Kenya, and South Africa were enrolled in the prevention of mother-to-child transmission Kesho Bora trial and counseled to either breastfeed exclusively and cease by 6 mo postpartum or formula feed exclusively. Maternal-reported morbidity (fever, diarrhea, and vomiting) and serious infectious events (SIEs) (gastroenteritis and lower respiratory tract infections) were investigated for 751 infants for 2 age periods (0-2.9 and 3-6 mo) by using generalized linear mixed models with breastfeeding as a time-dependent variable and adjustment for study site, maternal education, economic level, and cotrimoxazole prophylaxis.

**Results:** Reported morbidity was not significantly higher in nonbreastfed compared with breastfed infants [OR: 1.31 (95% CI: 0.97, 1.75) and 1.21 (0.90, 1.62) at 0-2.9 and 3-6 mo of age, respectively]. Between 0 and 2.9 mo of age, never-breastfed infants had increased risks of morbidity compared with those of infants who were exclusively breastfed (OR: 1.49; 95% CI: 1.01, 2.2; P = 0.042). The adjusted excess risk of SIEs in nonbreastfed infants was large between 0 and 2.9 mo (OR: 6.0; 95% CI: 2.2, 16.4; P = 0.001). Between 3 and 6 mo, the OR for SIEs was sensitive to the timing of breastfeeding status, i.e., 4.3 (95% CI: 1.2, 15.3; P = 0.02) when defined at end of monthly intervals and 2.0 (95% CI: 0.8, 5.0; P = 0.13) when defined at the beginning of intervals. Of 52 SIEs, 3 mothers reported changes in feeding mode during the SIE although none of the mothers ceased breastfeeding completely.

**Conclusions:** Not breastfeeding was associated with increased risk of serious infections especially between 0 and 2.9 mo of age.

**Abstract access**
**Editor’s notes**: Abstinence from breastfeeding or early weaning is known to be associated with higher mortality among infants born to women living with HIV. The risk of mother-to-child HIV transmission through breast-milk can be reduced by the use of antiretroviral therapies. Mothers living with HIV are advised to continue breastfeeding throughout infancy, while on therapy. The aim of this study was to investigate the association between breastfeeding and infection risk, accounting for reverse causality (i.e. mothers changing feeding mode in response to infant illness). Non-breastfed infants were at higher risk of serious infectious events than breastfed infants, as expected, and particularly among infants aged under three months. There was no evidence of a difference in reported morbidity. A qualitative assessment of the reverse causality found that some 94% of mothers reported not changing the feeding mode as a consequence of serious infectious events. The strengths of this study are that only HIV-exposed, but HIV-negative infants were included, and a range of sensitivity analyses were conducted. A limitation is that infant feeding data may be subject to reporting bias. This study has confirmed the findings of earlier research, and reassuringly found limited evidence to suggest reverse causality between breastfeeding and serious infectious outcomes.

**Countries**: Burkina Faso, Kenya, South Africa

**Region**: Africa

**Sub-categories**: Blood / body fluids and HIV prevention, preventing HIV infection in children

### 4. 15 million accessing treatment

**Interventions to promote adherence to antiretroviral therapy in Africa: a network meta-analysis.**


Background: Adherence to antiretroviral therapy (ART) is necessary for the improvement of the health of patients and for public health. We sought to determine the comparative effectiveness of different interventions for improving ART adherence in HIV-infected people living in Africa.

Methods: We searched for randomised trials of interventions to promote antiretroviral adherence within adults in Africa. We searched AMED, CINAHL, Embase, Medline (via PubMed), and ClinicalTrials.gov from inception to Oct 31, 2014, with the terms “HIV”, “ART”, “adherence”, and “Africa”. We created a network of the interventions by pooling the published and individual patients’ data for comparable treatments and comparing them across the individual interventions with Bayesian network meta-analyses. The primary outcome was adherence defined as the proportion of patients meeting trial defined criteria; the secondary endpoint was viral suppression.

Findings: We obtained data for 14 randomised controlled trials, with 7110 patients. Interventions included daily and weekly short message service (SMS; text message) messaging, calendars, peer supporters, alarms, counselling, and basic and enhanced standard of care (SOC). Compared with SOC, we found distinguishable improvement in self-reported adherence with enhanced SOC (odds ratio [OR] 1.46, 95% credibility interval [CrI] 1.06–1.98), weekly SMS messages (1.65, 1.25–2.18), counselling and SMS combined (2.07, 1.22–3.53), and treatment supporters (1.83, 1.36–2.45). We found no compelling evidence for the remaining interventions.
Results: were similar when using viral suppression as an outcome, although the network contained less evidence than that for adherence. **Treatment supporters with enhanced SOC (1.46, 1.09–1.97) and weekly SMS messages (1.55, 1.01–2.38) were significantly better than basic SOC.**

Interpretation: Several recommendations for improving adherence are unsupported by the available evidence. These findings can inform future intervention choices for improving ART adherence in low-income settings.

**Abstract access**

**Editor’s notes:** To maximise the impact of antiretroviral therapy (ART), people living with HIV should be diagnosed early, enrolled and retained in pre-ART care, initiated on ART and retained in ART care. Long-term adherence to achieve and maintain viral load suppression is the last step in the continuum of HIV care. Engagement along the complete treatment cascade will determine the long-term success of the global response to HIV.

A large number of potential programmes aimed at the improvement of engagement with care are available. While there is an urgent need for research on these programmes and on the effect of combined programmes, there is also the reality of a resource constrained environment. Network meta-analysis is a method to synthesise the evidence of programmes. The meta-analysis uses common comparators when these activities have not been compared head-to-head (resulting in indirect evidence), combined with evidence from head-to-head comparisons (direct evidence).

Using a network meta-analysis of randomized trials of programmes to improve ART adherence in Africa, the authors simultaneously compared eight groups of activities against standard care and against each other. The authors found that standard care augmented with intensified adherence counselling, or enhanced standard care, improved adherence to ART. Also weekly SMS messages, enhanced standard care combined with SMS, and enhanced standard care combined with having a treatment supporter were superior to standard care, with regards to self-reported adherence and viral suppression. The authors speculate that combinations of cognitive and behavioural programmes maximise the activity efficacy. Interestingly, their study found a large benefit for weekly but not for daily SMS messages. However the heterogeneity in the published treatment effects could be attributed to heterogeneity of the implemented programmes, especially of behavioural interventions. For example, the authors point out that there is a wide variability in the definition of standard care, and in the definition of treatment supporters.

The authors also note that several recommendations for improving adherence are unsupported by the evidence they examined using network meta-analysis.

**Countries:** Botswana, Cameroon, Kenya, Mozambique, Nigeria, South Africa, United Republic of Tanzania, Uganda, Zambia, Zimbabwe

**Region:** Africa

**Sub-categories:** Health care delivery

**Frontline health workers as brokers: provider perceptions, experiences and mitigating strategies to improve access to essential medicines in South Africa.**


Background: Front-line health providers have a unique role as brokers (patient advocates) between the health system and patients in ensuring access to medicines (ATM). ATM is a
fundamental component of health systems. This paper examines in a South African context supply- and demand- ATM barriers from the provider perspective using a five dimensional framework: availability (fit between existing resources and clients’ needs); accessibility (fit between physical location of healthcare and location of clients); accommodation (fit between the organisation of services and clients’ practical circumstances); acceptability (fit between clients’ and providers’ mutual expectations and appropriateness of care) and affordability (fit between cost of care and ability to pay).

Methods: This cross-sectional, qualitative study uses semi-structured interviews with nurses, pharmacy personnel and doctors. Thirty-six providers were purposively recruited from six public sector Community Health Centres in two districts in the Eastern Cape Province representing both rural and urban settings. Content analysis combined structured coding and grounded theory approaches. Finally, the five dimensional framework was applied to illustrate the interconnected facets of the issue.

Results: Factors perceived to affect ATM were identified. Availability of medicines was hampered by logistical bottlenecks in the medicines supply chain; poor public transport networks affected accessibility. Organization of disease programmes meshed poorly with the needs of patients with comorbidities and circular migrants who move between provinces searching for economic opportunities, proximity to services such as social grants and shopping centres influenced where patients obtain medicines. Acceptability was affected by, for example, HIV related stigma leading patients to seek distant services. Travel costs exacerbated by the interplay of several ATM barriers influenced affordability. Providers play a brokerage role by adopting flexible prescribing and dispensing for ‘stable’ patients and aligning clinic and social grant appointments to minimise clients’ routine costs. Occasionally they reported assisting patients with transport money.

Conclusion: All five ATM barriers are important and they interact in complex ways. Context-sensitive responses which minimise treatment interruption are needed. While broad-based changes encompassing all disease programmes to improve ATM are needed, a beginning could be to assess the appropriateness, feasibility and sustainability of existing brokerage mechanisms.

Abstract Full-text [free] access

Editor’s notes: The literature on health care providers and interactions with people accessing their services often casts the providers in a negative light. This paper focuses only on the providers and their observations on access to essential medicines in South Africa for treating HIV, TB, Type-2 diabetes and depression. The health care providers including nurses, doctors and pharmacy staff, talk of the challenges they face in providing care. Stock outs, transport problems, the mobility of their patients, who as a consequence miss appointments, and the poverty and hardship people face which hamper access to care. The authors provide a nuanced picture of the frustrations that the medical staff face as they try to provide care in an over-stretched public health system. Stories of their efforts to bend the rules to help mobile patients who need extra drugs while they travel, or the money given to help a very poor person get home are set alongside details of supply problems in remote rural clinics. The strength of this paper is that not only do the authors set out the barriers providers face in giving care, but also describe individual efforts made to improve things for people accessing services. These are not silent workers in the health service. They face challenges, yes, but they also have many ideas for how to make things better.

Countries: South Africa
Region: Africa
**Sub-categories:** Health care delivery, resources/impact/delivery, treatment

**Opportunities for improving the efficiency of paediatric HIV treatment programmes: lessons from the ARROW trial.**


**Objectives:** To conduct two economic analyses addressing whether to: routinely monitor HIV-infected children on antiretroviral therapy (ART) clinically or with laboratory tests; continue or stop cotrimoxazole prophylaxis when children become stabilized on ART.

**Design and methods:** The ARROW randomized trial investigated **alternative strategies to deliver paediatric ART and cotrimoxazole prophylaxis** in 1206 Ugandan/Zimbabwean children. Incremental cost-effectiveness and value of implementation analyses were undertaken. Scenario analyses investigated whether laboratory monitoring (CD4 tests for efficacy monitoring; haematology/biochemistry for toxicity) could be tailored and targeted to be delivered cost-effectively. **Cotrimoxazole use was examined in malaria-endemic and non-endemic settings.**

**Results:** Using all trial data, **clinical monitoring delivered similar health outcomes to routine laboratory monitoring, but at a reduced cost, so was cost-effective.** Continuing cotrimoxazole improved health outcomes at reduced costs. Restricting routine CD4 monitoring to after 52 weeks following ART initiation and removing toxicity testing was associated with an incremental cost-effectiveness ratio of $6084 per quality-adjusted life-year (QALY) across all age groups, but was much lower for older children (12+ years at initiation; incremental cost-effectiveness ratio = $769/QALY). **Committing resources to improve cotrimoxazole implementation appears cost-effective.** A healthcare system that could pay $600/QALY should be willing to spend up to $12.0 per patient-year to ensure continued provision of cotrimoxazole.

**Conclusion:** Clinically driven monitoring of ART is cost-effective in most circumstances. Routine laboratory monitoring is generally not cost-effective at current prices, except possibly CD4 testing amongst adolescents initiating ART. **Committing resources to ensure continued provision of cotrimoxazole in health facilities is more likely to represent an efficient use of resources.**

**Abstract access**

**Editor’s notes:** The authors set out to compare the cost-effectiveness of laboratory monitoring versus clinical monitoring of paediatric antiretroviral therapy (ART), and to determine the cost-effectiveness of continuing cotrimoxazole prophylaxis on children after being stabilised on ART. Using data from a trial in Uganda and Zimbabwe, they found that delivering ART with laboratory monitoring was generally more costly when compared with clinical monitoring. This was despite the two approaches having similar health outcomes. Laboratory monitoring was found not to be cost-effective, except potentially in cases of adolescents aged 12 and older (and without carrying out associated toxicity tests). The authors also found that discontinuing cotrimoxazole prophylaxis was both more costly and less effective than continuing provision. Reductions in cost of hospitalisations and prescriptions for malaria and other infections exceeded the costs of providing cotrimoxazole itself. **Cost-reductions were similar in both malaria-endemic and non-malaria-endemic settings.**
The questions addressed by this study are important because of the context of paediatric HIV in sub-Saharan Africa. As of 2013 only about 32% of children in need, in the region received ART. This background of poor health infrastructure and large gaps in paediatric treatment makes decision-making on limited resource allocation all the more important. The findings on the effectiveness of co-delivery of cotrimoxazole are further evidence of the need for governments and funders alike to think of effective and creative ways of integrating HIV care and treatment priorities within the wider health system.

This study should also be observed in light of changing national and international guidelines on detection of treatment failure. As of 2013, WHO has recommended viral load monitoring as the preferred method. When compared to CD4 testing, viral load monitoring tends to lead to better health outcomes but also requires sophisticated laboratory technology and highly trained technicians. Changing from CD4 to viral load monitoring may be unaffordable and logistically unfeasible in many settings.

Additionally, more countries in sub-Saharan Africa are rolling out point-of-care CD4 testing technologies. As more competitors in the field enter the point-of-care market, prices are likely to decrease. Although the authors have accounted for these future possibilities in their analysis, cost-effectiveness of monitoring of paediatric ART ought to be revisited at a later time once the costs related to point-of-care technologies have been more thoroughly understood.

Countries: Uganda, Zimbabwe
Region: Africa
Sub-categories: Health care delivery, resources/impact/development, treatment

5. Avoid TB deaths


Background: The duration of protection against tuberculosis provided by isoniazid preventive therapy is not known for human immunodeficiency virus (HIV)-infected individuals living in settings of medium tuberculosis incidence.

Methods: We conducted an individual-level analysis of participants in a cluster-randomized, phased-implementation trial of isoniazid preventive therapy. **HIV-infected patients who had positive tuberculin skin tests (TSTs) were followed until tuberculosis diagnosis, death, or administrative censoring.** Nelson-Aalen cumulative hazard plots were generated and hazards were compared using the log-rank test. Cox proportional hazards models were fitted to investigate factors associated with tuberculosis diagnosis.

Results: Between 2003 and 2009, **1954 patients with a positive TST were studied. Among these, 1601 (82%) initiated isoniazid.** Overall tuberculosis incidence was 1.39 per 100 person-years (PY); 0.53 per 100 PY in those who initiated isoniazid and 6.52 per 100 PY for those who did not (adjusted hazard ratio [aHR], 0.17; 95% confidence interval [CI], .11-.25). Receiving antiretroviral therapy at time of a positive TST was associated with a reduced risk of tuberculosis (aHR, 0.69; 95% CI, .48-1.00). **Nelson-Aalen plots of tuberculosis incidence showed a constant risk, with no acceleration in 7 years of follow-up for those initiating isoniazid preventive therapy.**
Conclusions: Isoniazid preventive therapy significantly reduced tuberculosis risk among HIV-infected patients with a positive TST. In a medium-prevalence setting, 6 months of isoniazid in HIV-infected patients with positive TST reduces tuberculosis risk over 7 years of follow-up, in contrast to results of studies in higher-burden settings in Africa.

Abstract access

Editor’s notes: Isoniazid preventive therapy (IPT) is a key component of WHO strategy to reduce the burden of tuberculosis among people living with HIV. In early randomised trials among people living with HIV, the duration of IPT was usually six months. This was consistently found to be effective in reducing TB incidence among people with a positive tuberculin skin test (TST). However, more recent studies from southern Africa have found that this protective effect wanes rapidly after the IPT course is completed. These studies have led to policy recommendations for continuous IPT for people living with HIV who are TST positive. In addition, mathematical modelling of trial data has suggested that IPT may not "cure" latent TB infection in people living with HIV.

There are few data from settings with lower TB transmission documenting the durability of short-course IPT among people living with HIV. This paper reports long-term follow-up among people living with HIV who received IPT in the THRio study in Brazil, a medium TB burden setting. The data provides reassurance that a six-month course of IPT gives durable protection against TB among people living with HIV. Nonetheless, there is a need for implementation of shorter, effective TB preventive therapy regimens, which are less arduous for people and simpler for health services to deliver.

Countries: Brazil
Region: Latin America
Sub-categories: co-morbidity

Incidence of HIV-associated tuberculosis among individuals taking combination antiretroviral therapy: a systematic review and meta-analysis.


Background: Knowledge of tuberculosis incidence and associated factors is required for the development and evaluation of strategies to reduce the burden of HIV-associated tuberculosis.

Methods: Systematic literature review and meta-analysis of tuberculosis incidence rates among HIV-infected individuals taking combination antiretroviral therapy.

Results: From PubMed, EMBASE and Global Index Medicus databases, 42 papers describing 43 cohorts (32 from high/intermediate and 11 from low tuberculosis burden settings) were included in the qualitative review and 33 in the quantitative review. Cohorts from high/intermediate burden settings were smaller in size, had lower median CD4 cell counts at study entry and fewer person-years of follow up. Tuberculosis incidence rates were higher in studies from sub-Saharan Africa and from World Bank low/middle income countries. Tuberculosis incidence rates decreased with increasing CD4 count at study entry and duration on combination antiretroviral therapy. Summary estimates of tuberculosis incidence among individuals on combination antiretroviral therapy were higher for cohorts from high/intermediate burden settings compared to those from the low tuberculosis burden settings (4.17 per 100 person-years [95% Confidence Interval (CI) 3.39-5.14 per 100 person-years] vs. 0.4 per 100 person-years [95% CI 0.23-0.69 per 100 person-years]) with significant heterogeneity observed between the studies.
Conclusions: Tuberculosis incidence rates were high among individuals on combination antiretroviral therapy in high/intermediate burden settings. **Interventions to prevent tuberculosis in this population should address geographical, socioeconomic and individual factors such as low CD4 counts and prior history of tuberculosis.**

Abstract  Full-text [free] access

**Editor’s notes:** This systematic review and meta-analysis looks at tuberculosis (TB) incidence rates among adults living with HIV on antiretroviral treatment (ART). The review reinforces and quantifies what we already know about the disparities between low-burden and high-burden settings. TB incidence rates in high and intermediate burden settings are ten times higher than those in low burden settings.

The authors draw attention to the need for implementation of programmes that address the social determinants of TB. Low socio-economic conditions are associated with higher TB incidence rates in individuals on ART. Interestingly, the meta-analysis found that TB incidence rates were higher among individuals on ART who had a previous history of TB, than individuals who did not have a history of previous TB. The epidemiological association between previous TB treatment and active TB was one of the foundations for the emphasis on case retention and cure rates with the Directly Observed Treatment, Short-Course (DOTS) strategy. Yet prevalence surveys conducted in Zimbabwe, South Africa and Zambia in the pre-ART and early ART era did not find an association between a history of previous TB and prevalent active undiagnosed TB in individuals living with HIV. The finding from this meta-analysis suggests that individuals on ART are now surviving long enough to develop recurrent TB disease.

The overall message of the study is that ART alone is not sufficient to reduce TB incidence in high HIV prevalence settings. Additional strategies are required to prevent TB focussing on individuals with low CD4 counts, a history of previous TB disease and people who have recently initiated ART.

**Countries:** Brazil, Canada, China, Province of Taiwan, Cote d’Ivoire, Denmark, Ethiopia, France, India, Senegal, South Africa, Spain, United Republic of Tanzania, Uganda, United Kingdom, United States of America

**Region:** Africa, Asia, Europe, Northern America

**Sub-categories:** Co-morbidity, epidemiology, people living with HIV, treatment

**Effects of vaccination on invasive pneumococcal disease in South Africa.**


Background: In South Africa, a 7-valent pneumococcal conjugate vaccine (PCV7) was introduced in 2009 with a three-dose schedule for infants at 6, 14, and 36 weeks of age; a 13-valent vaccine (PCV13) replaced PCV7 in 2011. In 2012, it was estimated that 81% of 12-month-old children had received three doses of vaccine. We assessed the effect of vaccination on invasive pneumococcal disease.

Methods: We conducted national, active, laboratory-based surveillance for invasive pneumococcal disease. We calculated the change in the incidence of the disease from a prevaccine (baseline) period (2005 through 2008) to postvaccine years 2011 and 2012, with a focus on high-risk age groups.
Results: Surveillance identified 35,192 cases of invasive pneumococcal disease. The rates among children younger than 2 years of age declined from 54.8 to 17.0 cases per 100,000 person-years from the baseline period to 2012, including a decline from 32.1 to 3.4 cases per 100,000 person-years in disease caused by PCV7 serotypes (-89%; 95% confidence interval [CI], -92 to -86). Among children not infected with the human immunodeficiency virus (HIV), the estimated incidence of invasive pneumococcal disease caused by PCV7 serotypes decreased by 85% (95% CI, -89 to -79), whereas disease caused by nonvaccine serotypes increased by 33% (95% CI, 15 to 48). Among adults 25 to 44 years of age, the rate of PCV7-serotype disease declined by 57% (95% CI, -63 to -50), from 3.7 to 1.6 cases per 100,000 person-years.

Conclusions: Rates of invasive pneumococcal disease among children in South Africa fell substantially by 2012. Reductions in the rates of disease caused by PCV7 serotypes among both children and adults most likely reflect the direct and indirect effects of vaccination.

Abstract Full-text [free] access

Editor's notes: There has been a marked reduction in invasive pneumococcal disease in high-income settings following the roll-out of pneumococcal conjugate vaccine. The reduction in incidence of pneumococcal disease has been observed not just among vaccinated infants but also among older children and adults, indicating herd immunity. This study is the first to report on the population impact of pneumococcal vaccination given at six weeks, 14 weeks and nine months of age in an African setting with a high prevalence of HIV and high antiretroviral therapy coverage. Following the introduction of infant pneumococcal vaccination in 2009, the incidence of laboratory reported invasive pneumococcal disease (defined as hospitalised person with positive cultures from sterile sites) declined by 89% for pneumococcal conjugate vaccine -7 (PCV-7) serotypes. A reduction in the incidence of non-vaccine serotypes of 20% indicates that some, but not all of this reduction may be due to improvements in HIV care and increasing antiretroviral therapy coverage. As observed in high-income settings the benefits were seen not just in infants but also in older children and adults. Reassuringly, a reduced incidence of pneumococcal disease was found in individuals living with HIV and in people who did not have the disease. While there was some indication that serotype replacement may become a future problem (small increase in invasive diseases caused by non-vaccine serotypes in HIV negative infants) longer follow-up data is required to fully explore this issue.

Countries: South Africa
Region: Africa
Sub-categories: Comorbidity, epidemiology, national responses

6. Close the resource gap

Multi-country analysis of treatment costs for HIV/AIDS (MATCH): facility-level ART unit cost analysis in Ethiopia, Malawi, Rwanda, South Africa and Zambia.


Background: Today's uncertain HIV funding landscape threatens to slow progress towards treatment goals. Understanding the costs of antiretroviral therapy (ART) will be essential for governments to make informed policy decisions about the pace of scale-up under the 2013
WHO HIV Treatment Guidelines, which increase the number of people eligible for treatment from 17.6 million to 28.6 million. The study presented here is one of the largest of its kind and the first to describe the facility-level cost of ART in a random sample of facilities in Ethiopia, Malawi, Rwanda, South Africa and Zambia.

Methods & Findings: In 2010-2011, comprehensive data on one year of facility-level ART costs and patient outcomes were collected from 161 facilities, selected using stratified random sampling. Overall, facility-level ART costs were significantly lower than expected in four of the five countries, with a simple average of $208 per patient-year (ppy) across Ethiopia, Malawi, Rwanda and Zambia. Costs were higher in South Africa, at $682 ppy. This included medications, laboratory services, direct and indirect personnel, patient support, equipment and administrative services. Facilities demonstrated the ability to retain patients alive and on treatment at these costs, although outcomes for established patients (2-8% annual loss to follow-up or death) were better than outcomes for new patients in their first year of ART (77-95% alive and on treatment).

Conclusions: This study illustrated that the facility-level costs of ART are lower than previously understood in these five countries. While limitations must be considered, and costs will vary across countries, this suggests that expanded treatment coverage may be affordable. Further research is needed to understand investment costs of treatment scale-up, non-facility costs and opportunities for more efficient resource allocation.

Abstract Full-text [free] access

Editor’s notes: This paper describes the facility-level costs for antiretroviral therapy (ART) delivery in 161 facilities across five countries. The scale of this study is impressive. At 161 facilities, it is one of the largest existing evaluations of facility-level costs for delivering ART. Collecting detailed cost data is a time- and resource-intensive process, and there is remarkable value in this quantity of cost data being made available.

The results are also surprising. The average cost for ART at the facility level in four of five countries ($208 per person per year) is consistently much lower than previously understood. Primary costing studies in low- and middle-income settings typically find some level of inconsistency between facilities, reflecting room to improve efficiency. This study found more variation in South Africa than in other settings, but relatively little variation overall. It would be interesting to find out in more detail whether this was a function of missing data, or whether the facilities included in the analysis were consistently efficient. If the latter, this may be an indication of improving efficiency in delivery of HIV treatment services.

The most exciting outcome from this study is the low costs found across settings. A number of existing studies of ART costs, all published between 2004-2008, find average facility costs ranging from $650 to $1000 per person, per year. The authors explain their lower costs as a reflection of reduced ART drug prices over the last ten years. Such a dramatic drop in costs is encouraging, particularly in the context of current efforts to expand access to ART.

Countries: Ethiopia, Malawi, Rwanda, South Africa and Zambia
Region: Africa
Sub-categories: Health care delivery, resources/ impact/ development, treatment
7. Eliminate gender inequalities

The impact of SASA!, a community mobilization intervention, on reported HIV-related risk behaviours and relationship dynamics in Kampala, Uganda.


Introduction: Intimate partner violence (IPV) violates women's human rights, and it is a serious public health concern associated with increased HIV risk. SASA!, a phased community mobilization intervention, engages communities to prevent IPV and promote gender equity. The SASA! study assessed the community-level impact of SASA! on reported HIV-related risk behaviours and relationship dynamics.

Methods: Data were collected as part of a cluster randomized controlled trial conducted between 2007 and 2012 in eight communities in Kampala. An adjusted cluster-level intention to treat analysis, compares secondary outcomes in intervention and control communities at follow-up. The qualitative evaluation explored participants’ subjective experience of SASA!. A total of 82 in-depth interviews were audio recorded at follow-up, transcribed verbatim and analyzed using thematic analysis.

Results: Men in intervention communities were significantly more likely than controls to report a broad range of HIV-protective behaviours, including higher levels of condom use (aRR 2.03, 95% CI 1.22-3.39), HIV testing (aRR 1.50, 95% CI 1.13-2.00) and fewer concurrent partners (aRR 0.60, 95% CI 0.37-0.97). They were also more likely to report increased joint decision-making (aRR 1.92, 95% CI 1.27-2.91), greater male participation in household tasks (aRR 1.48, 95% CI 1.09-2.01), more open communication and greater appreciation of their partner's work inside (aRR 1.31, 95% CI 1.04-1.66) and outside (aRR 1.49, 95% CI 1.08-2.06) the home. For women, all outcomes were in the hypothesized direction, but effect sizes were smaller. Only some achieved statistical significance. Women in intervention communities were significantly more likely to report being able to refuse sex with their partners (aRR 1.16, 95% CI 1.00-1.35), joint decision-making (aRR 1.37, 95% CI 1.06-1.78) and more open communication on a number of indicators. Qualitative interviews suggest that shifts operated through broader improvements in relationships, including increased trust and cooperation, participants’ greater awareness of the connections between HIV and IPV and their resultant desire to improve their relationships. Barriers to change include partial uptake of SASA!, partner resistance, fear and entrenched previous beliefs.

Conclusions: SASA! impacted positively on reported HIV-related risk behaviours and relationship dynamics at a community level, especially among men. Social change programmes focusing on IPV and gender equity could play an important role in HIV prevention efforts.

Abstract Full-text [free] access

Editor’s notes: This cluster randomised trial adds to the increasing evidence that participatory, gender transformative violence prevention programmes can impact intimate partner violence and HIV-related risk behaviour. The trial evaluated the impact of SASA!, a phased community mobilisation programme that seeks to prevent intimate partner violence and to reduce HIV-related behaviours at the community level. Results illustrated that SASA! was associated with lower, past year experience of physical and sexual intimate partner violence among women and lower levels of sexual concurrency among men. In this paper, the authors report the secondary outcomes of the trial relating to HIV-related risk behaviours and several indicators of relationship dynamics. They also report
findings from the qualitative evaluation which suggest that SASA! has the potential to improve relationship dynamics and to reduce HIV-related risk behaviours within intimate partnerships. The impact was greater in men, which may reflect respondent bias. However, given its context, in which patriarchy is dominant, the results of this study are encouraging. SASA! may make men more cognisant of what they should or could be doing to foster more equitable relationships. Changes in male behaviour have the potential to improve relationship dynamics and reduce HIV-related risk behaviours.

Countries: Uganda
Region: Africa

Sub-categories: Civil society and community responses/resilience, gender, structural determinants and vulnerability

Women with HIV: gender violence and suicidal ideation

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Objective: To analyze the relationship between gender violence and suicidal ideation in women with HIV.

Methods: A cross-sectional study with 161 users of specialized HIV/AIDS care services. The study investigated the presence of gender violence through the Brazilian version of the World Health Organization Violence against Women instrument, and suicidal ideation through the Suicidal Ideation Questionnaire. Statistical analyses were performed with the SPSS software, using the Chi-square test and Poisson multiple regression model.

Results: Eighty-two women with HIV reported suicidal ideation (50.0%), 78 (95.0%) of whom had suffered gender violence. Age at first sexual intercourse < 15 years old, high number of children, poverty, living with HIV for long, and presence of violence were statistically associated with suicidal ideation. Women who suffered gender violence showed 5.7 times more risk of manifesting suicidal ideation.

Conclusions: Women with HIV showed a high prevalence to gender violence and suicidal ideation. Understanding the relationship between these two grievances may contribute to the comprehensive care of these women and implementation of actions to prevent violence and suicide.

Abstract  Full-text [free] access

Editor’s notes: The HIV epidemic in Brazil is becoming increasingly feminized. The male to female ratio of HIV infections has decreased from 26 to 1.5 men for every woman, over the past 10 years. Within the HIV field, there has been growing recognition of the mental health impacts of HIV infection, and the importance of considering how best to address this issue, as part of service provision. Similarly, there has been growing recognition within the violence field, that experiences of violence from a partner has both short and long term mental health impacts. Women who have violent partners may be at greater risk of contracting HIV, and be at risk of violence following disclosure. This paper illustrates the ways in which these issues cluster. The study finds that women living with HIV who had a history of violence are far more likely to report being HIV positive. The findings illustrate the need for HIV services to be able to both support women with mental health support needs, and support women who have a history of violence. The findings suggest that HIV counsellors need to be able to discuss issues of depression, suicidal ideation and violence, and potentially facilitate referral to specialized services in each area.
8. Strengthening HIV integration

A systematic review of individual and contextual factors affecting ART initiation, adherence, and retention for HIV-infected pregnant and postpartum women.


Background: Despite progress reducing maternal mortality, HIV-related maternal deaths remain high, accounting, for example, for up to 24 percent of all pregnancy-related deaths in sub-Saharan Africa. Antiretroviral therapy (ART) is effective in improving outcomes among HIV-infected pregnant and postpartum women, yet rates of initiation, adherence, and retention remain low. This systematic literature review synthesized evidence about individual and contextual factors affecting ART use among HIV-infected pregnant and postpartum women.

Methods: Searches were conducted for studies addressing the population (HIV-infected pregnant and postpartum women), intervention (ART), and outcomes of interest (initiation, adherence, and retention). Quantitative and qualitative studies published in English since January 2008 were included. Individual and contextual enablers and barriers to ART use were extracted and organized thematically within a framework of individual, interpersonal, community, and structural categories.

Results: Thirty-four studies were included in the review. Individual-level factors included both those within and outside a woman's awareness and control (e.g., commitment to child's health or age). Individual-level barriers included poor understanding of HIV, ART, and prevention of mother-to-child transmission, and difficulty managing practical demands of ART. At an interpersonal level, disclosure to a spouse and spousal involvement in treatment were associated with improved initiation, adherence, and retention. Fear of negative consequences was a barrier to disclosure. At a community level, stigma was a major barrier. Key structural barriers and enablers were related to health system use and engagement, including access to services and health worker attitudes.

Conclusions: To be successful, programs seeking to expand access to and continued use of ART by integrating maternal health and HIV services must identify and address the relevant barriers and enablers in their own context that are described in this review. Further research on this population, including those who drop out of or never access health services, is needed to inform effective implementation.

Abstract Full-text [free] access

Editor's notes: This systematic review is one of three by the same team, related to HIV and maternal mortality. The review findings illustrate that the individual and contextual factors which affect antiretroviral therapy (ART) initiation, adherence and retention for pregnant/postpartum women living with HIV are numerous. Fears over disclosure, and consequent stigma and discrimination feature in many of the studies reviewed. Practical barriers might be overcome, by making services more accessible. The lack of knowledge about HIV and treatment among some women may be addressed
through information campaigns. However, the fear of negative consequences as a result of disclosure, even to health workers, presents significant barriers to care. This is something that is of particular note as Option B+ is rolled out. An important strength of this review is the combination of qualitative and quantitative studies. The meticulous description of the approach to the review is also welcome. The authors’ call for ‘consistent, standardised and appropriate measures of adherence and retention’ with a ‘longitudinal component’, is a valuable suggestion as the performance of countries in providing Option B+ begins to be compared.

**Countries:** Australia, Brazil, France, Ghana, Kenya, Malawi, Nigeria, Rwanda, South Africa, Uganda, United Republic of Tanzania, United States of America, Zambia

**Region:** Africa, Asia, Europe, Northern America, Latin America

**Sub-categories:** Treatment, health care delivery, gender, people living with HIV