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

1. **Reduce sexual transmission**
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   - Female migrants may be more at risk of HIV in Kazakhstan
   - DMPA contraception users more likely than NET-EN users to acquire HIV in South Africa
   - Building a PrEP bridge: is it cost-effective?
   - Wide variation in national HIV policies associated with HIV testing and treatment across six African countries

2. **Eliminate new HIV infections among children**
   - One in 10 mothers living with HIV are unaware of their status
   - Benefits to women and newborns by integrating HIV and ANC services

3. **15 million accessing treatment**
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   - Single dose nevirapine for PMTCT does not jeopardise future NNRTI-based ART in children
   - ART outcomes not improved by medication monitors plus text message reminders
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   - Agricultural and microfinance programmes might be part of the mix to achieve the virologic suppression goal

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   - Regressive laws on same sex relationships increases stigma and reduces health service use
7. **Strengthening HIV integration**

- Leveraging an HIV-specific quality improvement programme to realise system-wide benefits in Haiti
- Community health workers can improve emotional wellbeing of mothers in a high HIV prevalence setting

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HIV this month, published by UNAIDS, is a selective scan of new HIV-related information found in scientific journals. The Editors of HIV this month interpret original abstracts and provide editorial comment, so that information may be easily understood by people responding to the HIV epidemic in many diverse settings. The selection of material, its abridgement and other editorial changes, and also the original editorial comment are the responsibility of the Editors and do not represent any official statement of UNAIDS. It should be noted that (except for open access journals, e.g. PLoS) the authors and/or publishers retain copyright in the original published material to which HIV this month refers.
1. Reduce sexual transmission

Length of secondary schooling and risk of HIV infection in Botswana: evidence from a natural experiment.


Background: An estimated 2.1 million individuals are newly infected with HIV every year. Cross-sectional and longitudinal studies have reported conflicting evidence for the association between education and HIV risk, and no randomised trial has identified a causal effect for education on HIV incidence. **We aimed to use a policy reform in secondary schooling in Botswana to identify the causal effect of length of schooling on new HIV infection.**

Methods: Data for HIV biomarkers and demographics were obtained from the **nationally representative household 2004 and 2008 Botswana AIDS Impact Surveys (N=7018).** In 1996, Botswana reformed the grade structure of secondary school, expanding access to grade ten and increasing educational attainment for affected cohorts. **Using exposure to the policy reform as an instrumental variable, we used two-stage least squares to estimate the causal effect of years of schooling on the cumulative probability that an individual contracted HIV up to their age at the time of the survey.** We also assessed the cost-effectiveness of secondary schooling as an HIV prevention intervention in comparison to other established interventions.

Findings: **Each additional year of secondary schooling caused by the policy change led to an absolute reduction in the cumulative risk of HIV infection of 8.1 percentage points (p=0.008), relative to a baseline prevalence of 25.5% in the pre-reform 1980 birth cohort. Effects were particularly large in women (11.6 percentage points, p=0.046).** Results were robust to a wide array of sensitivity analyses. **Secondary school was cost effective as an HIV prevention intervention by standard metrics** (cost per HIV infection averted was US$27 753).

Interpretation: **Additional years of secondary schooling had a large protective effect against HIV risk in Botswana, particularly for women. Increasing progression through secondary school could be a cost-effective HIV prevention measure in HIV-endemic settings, in addition to yielding other societal benefits.**

Abstract Full-text [free] access

**Editor’s notes:** There is conflicting evidence on the association between education and HIV risk, and little causal evidence. Observational studies are limited by strong confounding by factors such as socioeconomic status and psychological traits, while previous randomised trials have been underpowered for HIV incidence. A policy reform in Botswana in 1996 provided a unique opportunity to assess this question. The policy affected specific birth cohorts and meant that the average number of years of schooling increased by nearly one year. The reform was unlikely to have affected HIV risk through mechanisms other than schooling itself. It therefore constitutes a natural experiment to estimate the causal effect of schooling on the risk of HIV infection, through comparison of birth cohorts exposed to the policy reform versus people unexposed. The authors found that, for each additional year of schooling induced by the reform, there was an 8.1 percentage point reduction in the risk of HIV infection. The effect was particularly strong among women, with an 11.6 percentage point reduction. These results translated to a cost of $27 753 per HIV infection averted. Secondary schooling is therefore more expensive than circumcision or treatment as prevention, but of similar
cost-effectiveness to the upper range of estimates for pre-exposure prophylaxis. In addition, schooling offers other benefits beyond the reduction of HIV transmission.

Migrant workers in Kazakhstan: gender differences in HIV knowledge and sexual risk behaviors.


This study compares sexual risk behaviors among male and female migrant market vendors in Almaty, Kazakhstan. From the Barakholka Market, 209 male and 213 female market vendors were randomly recruited. Self-reported data were collected through standardized face-to-face interviews. Dry blood spot was used as specimen for syphilis testing. Propensity score stratification was used to estimate adjusted prevalence or rate ratios by gender. Compared to male migrant workers, females had lower HIV knowledge and were less likely to have multiple sexual partners. There was no evidence of a gender difference for prevalence of syphilis, condom use with unsteady partners, and safe sex communication between couples. Associations between mobility patterns and engagement in multiple sexual partnerships were stronger among women than men. Efforts should be made to mitigate the gender differential in HIV knowledge among migrants, especially women. Such efforts need to be implemented in both home and host countries.

Abstract Full-text [free] access

Editor’s notes: Migration and mobility have been shown to be contributing factors to increased risk of HIV around the world. This is due to a number of factors, but most common are lack of social support, little or no access to services, and language and legal issues. Depending on socio-economic contexts, women and men will often leave their homes for periods of time to trade or work in agriculture or construction in other domestic or international locations. This paper examines the relationship between gender and sexual risk behaviours in Almaty, the financial capital of Kazakhstan. Kazakhstan, and Almaty in particular, is a hub for trade migrants from all over Central Asia. The paper notes the lack of accurate statistics for gender distribution among migrants, but estimates indicate high proportion are women. Overall, the study found that the migrant population surveyed was more likely to have multiple sexual partners than the general population, although the data used as the general population comparison was somewhat dated. Women were less likely to be educated about HIV than men, and while also less likely to have multiple sexual partners than men, the partnerships they did have were closely linked to their mobility and the time spent at market. This study provides important insights into the HIV and sexual risk contexts in this region, and highlights the importance of continuing research there in order to inform HIV prevention and care programmes which can better support population needs.

Risk of HIV-1 acquisition among women who use different types of injectable progestin contraception in South Africa: a prospective cohort study.


Background: Several observational studies have reported that HIV-1 acquisition seems to be higher in women who use depot medroxyprogesterone acetate (DMPA) than in those who do not use hormonal
contraception. **We aimed to assess whether two injectable progestin-only contraceptives, DMPA and norethisterone enanthate (NET-EN), confer different risks of HIV-1 acquisition.**

**Methods:** We included data from South African women who used injectable contraception while participating in the VOICE study, a multisite, randomised, placebo-controlled trial that investigated the safety and efficacy of three formulations of tenofovir for prevention of HIV-1 infection in women between Sept 9, 2009, and Aug 13, 2012. Women were assessed monthly for contraceptive use and incident infection. We estimated the difference in incident HIV-1 infection between DMPA and NET-EN users by Cox proportional hazards regression analyses in this prospective cohort. The VOICE trial is registered with ClinicalTrials.gov, NCT00705679.

**Findings:** 3141 South African women using injectable contraception were included in the present analysis: 1788 (56.9%) solely used DMPA, 1097 (34.9%) solely used NET-EN, and 256 (8.2%) used both injectable types at different times during follow-up. During 2733.7 person-years of follow-up, 207 incident HIV-1 infections occurred (incidence 7.57 per 100 person-years, 95% CI 6.61-8.68). **Risk of HIV-1 acquisition was higher among DMPA users** (incidence 8.62 per 100 person-years, 95% CI 7.35-10.11) than among NET-EN users (5.67 per 100 person-years, 4.37-7.38; hazard ratio 1.53, 95% CI 1.12-2.08; p=0.007). This association persisted when adjusted for potential confounding variables (adjusted hazard ratio [aHR] 1.41, 95% CI 1.06-1.89; p=0.02). Among women seropositive for herpes simplex virus type 2 (HSV-2) at enrolment, the aHR was 2.02 (95% CI 1.26-3.24) compared with 1.09 (0.78-1.52) for HSV-2-seronegative women (pinteraction=0.07).

**Interpretation:** Although moderate associations in observational analyses should be interpreted with caution, these findings suggest that NET-EN might be an alternative injectable drug with a lower HIV risk than DMPA in high HIV-1 incidence settings where NET-EN is available.

**Abstract access**

**Editor’s notes:** In eastern and southern Africa, injectable methods are the most popular contraceptives. But evidence that the injectable progestin depot medroxyprogesterone acetate (DMPA) is associated with an increased risk of HIV-1 acquisition means that alternative injectable contraceptive methods are necessary. This large prospective study used data from the VOICE HIV prevention trial, analysing data from South Africa on 3141 women who had used one of two progestin methods for contraception. HIV incidence was high in the population (7.57/100 person-years overall), and participants who used DMPA were 40% more likely to become HIV positive than women who used norethisterone enanthate (NET-EN) after adjustment for demographic and behavioural confounding variables. Strengths of this study include the comparability across women using progestin methods, and its frequent follow up visits to assess HIV status, contraception use, sexual behaviour and the presence of reproductive tract infections. The results suggest NET-EN might be an alternative injectable contraceptive with a lower risk for HIV-1 acquisition than DMPA.

**Cost-effectiveness of pre-exposure prophylaxis targeted to high-risk serodiscordant couples as a bridge to sustained ART use in Kampala, Uganda.**


**Introduction:** Despite scale-up of antiretroviral therapy (ART) for treating HIV-positive persons, HIV incidence remains elevated among those at high risk such as persons in serodiscordant partnerships. Antiretrovirals taken by HIV-negative persons as pre-exposure prophylaxis (PrEP) has the potential to avert infections in individuals in serodiscordant partnerships. **Evaluating the cost-effectiveness of**
implementing time-limited PrEP as a short-term bridge during the first six months of ART for the HIV-positive partner to prevent HIV transmission compared to increasing ART coverage is crucial to informing policy-makers considering PrEP implementation.

Methods: To estimate the real world delivery costs of PrEP, we conducted micro-costing and time and motion analyses in an open-label prospective study of PrEP and ART delivery targeted to high-risk serodiscordant couples in Uganda (the Partners Demonstration Project). The cost (in USD, in 2012) of PrEP and ART for serodiscordant couples was assessed, with and without research components, in the study setting. Using Ministry of Health costs, the cost of PrEP and ART provision within a government programme was estimated, as was the cost of providing PrEP in addition to ART. We parameterized an HIV transmission model to estimate the health and economic impacts of 1) PrEP and ART targeted to high-risk serodiscordant couples in the context of current ART use and 2) increasing ART coverage to 55% of HIV-positive persons with CD4 ≤500 cells/µL without PrEP. The incremental cost-effectiveness ratios (ICERs) per HIV infection and disability-adjusted life year (DALY) averted were calculated over 10 years.

Results: The annual cost of PrEP and ART delivery for serodiscordant couples was $1058 per couple in the study setting and $453 in the government setting. The portion of the programme cost due to PrEP was $408 and $92 per couple per year in the study and government settings, respectively. Over 10 years, a programme of PrEP and ART for high-risk serodiscordant couples was projected to avert 43% of HIV infections compared to current practice with an ICER of $1340 per infection averted. This was comparable to ART expansion alone, which would avert 37% of infections with an ICER of $1452.

Conclusions: Using Uganda's gross domestic product per capita of $1681 as a threshold, PrEP and ART for high-risk persons have the potential for synergistic action and are cost-effective in preventing HIV infections in high prevalence settings. The annual cost of PrEP in this programme is less than $100 per serodiscordant couple if implemented in public clinics.

Abstract Full-text [free] access

Editor’s notes: Antiretroviral therapy (ART) is an effective way of preventing onward transmission of HIV. However, HIV-negative partners in serodiscordant couples remain at risk during the period before the HIV-positive partner starts ART and in the period between treatment initiation and virologic suppression. Time-limited PrEP is proposed as a means to bridge this gap and reduce the risk of transmission. This study looked at the cost-effectiveness of introducing PrEP in this context. It compared that to the cost-effectiveness of increasing ART coverage. The study also looked at costs in the study clinic which was private, as well as modelled to estimate cost of delivery through the Ministry of Health.

One of the study’s strengths is that it is based on a micro-costing exercise, which had not been done before, on the programmatic costs of PrEP implementation. This is very important as cost-effectiveness studies on this topic can often be based on cost assumptions that are unrepresentative or outdated. This data was then used to model the different scenarios using a dynamic transmission model.

The study found that, in terms of infections averted, combining PrEP and ART and ART scale-up were both very cost-effective. But combining PrEP and ART averted more infections than ART scale-up in relation to the baseline (43% versus 37%, respectively). When looking at disability-adjusted life years (DALYs) averted, combining ART and PrEP was not shown to be cost-effective, but would avert
62% more DALYs than baseline. ART scale-up on the other hand was very cost-effective and would avert 60% more DALYs than baseline.

It is important to note that the study is reliant on a relatively small sample. It seems that only one clinic was sampled and a relatively small number of visits were timed to determine staff costs. Further, the study makes certain assumptions that are left unexplained, such as including the costs of viral load point-of-care tests, which are largely unknown as the technology has yet to be implemented. However, despite these shortfalls, the study is significant because it could help to inform country guidelines on how to target PrEP for specific key populations, in this case serodiscordant couples. A worthwhile follow-up of this study would look at patient-level costs associated with this PrEP delivery strategy, which could potentially have an effect on uptake, and which may vary between key populations.

A comparative analysis of national HIV policies in six African countries with generalized epidemics.


Objective: To compare national human immunodeficiency virus (HIV) policies influencing access to HIV testing and treatment services in six sub-Saharan African countries.

Methods: We reviewed HIV policies as part of a multi-country study on adult mortality in sub-Saharan Africa. A policy extraction tool was developed and used to review national HIV policy documents and guidelines published in Kenya, Malawi, South Africa, Uganda, the United Republic of Tanzania and Zimbabwe between 2003 and 2013. Key informant interviews helped to fill gaps in findings. National policies were categorized according to whether they explicitly or implicitly adhered to 54 policy indicators, identified through literature and expert reviews. We also compared the national policies with World Health Organization (WHO) guidance.

Findings: There was wide variation in policies between countries; each country was progressive in some areas and not in others. Malawi was particularly advanced in promoting rapid initiation of antiretroviral therapy. However, no country had a consistently enabling policy context expected to increase access to care and prevent attrition. Countries went beyond WHO guidance in certain areas and key informants reported that practice often surpassed policy.

Conclusion: Evaluating the impact of policy differences on access to care and health outcomes among people living with HIV is challenging. Certain policies will exert more influence than others and official policies are not always implemented. Future research should assess the extent of policy implementation and link these findings with HIV outcomes.

Abstract Full-text [free] access

Editor’s notes: Despite evidence on reduction in HIV attributable mortality, concerns still remain on the high attrition rates across the diagnosis-to-treatment cascade. This paper uses a comparative policy analysis to track differences in national HIV policy responses to the HIV epidemic. The methodology used is notable as it offers a helpful conceptual framework for the HIV policy and service factors influencing specific differences in HIV-associated adult mortality across the diagnosis-to-treatment cascade.
The range of policies between countries was unexpected, given the explanation offered by the authors that African countries tend to adopt standards and guidance from WHO. Furthermore, while countries showed progressive elements, no country had the comprehensive policy context necessary for a decisive impact on service access. Important differences were also noted in the influential weight given to some policies, in the timing of policy implementation in some indicators, and in whether WHO national standards were or were not adopted by countries. These findings are particularly useful in better understanding the incentives and barriers to accessing antiretroviral therapy in different contexts.

2. Eliminate new HIV infections among children

Missed opportunities along the prevention of mother-to-child transmission services cascade in South Africa: uptake, determinants, and attributable risk (the SAPMTCTE).


Objectives: We examined uptake of prevention of mother-to-child HIV transmission (PMTCT) services, predictors of missed opportunities, and infant HIV transmission attributable to missed opportunities along the PMTCT cascade across South Africa.

Methods: A cross-sectional survey was conducted among 4-8 week old infants receiving first immunisations in 580 nationally representative public health facilities in 2010. This included maternal interviews and testing infants’ dried blood spots for HIV. A weighted analysis was performed to assess uptake of antenatal and perinatal PMTCT services along the PMTCT cascade (namely: maternal HIV testing, CD4 count test/result, and receiving maternal and infant antiretroviral treatment) and predictors of dropout. The population attributable fraction associated with dropouts at each service point are estimated.

Results: Of 9803 mothers included, 31.7% were HIV-positive as identified by reactive infant antibody tests. Of these 80.4% received some form of maternal and infant antiretroviral treatment. More than a third (34.9%) of mothers dropped out from one or more steps in the PMTCT service cascade. In a multivariable analysis, the following characteristics were associated with increased dropout from the PMTCT cascade: adolescent (<20 years) mothers, low socioeconomic score, low education level, primiparous mothers, delayed first antenatal visit, homebirth, and non-disclosure of HIV status. Adolescent mothers were twice (adjusted odds ratio: 2.2, 95% confidence interval: 1.5-3.3) as likely to be unaware of their HIV-positive status and had a significantly higher rate (85.2%) of unplanned pregnancies compared to adults aged ≥20 years (55.5%, p = 0.0001). A third (33.8%) of infant HIV infections were attributable to dropout in one or more steps in the cascade.

Conclusion: A third of transmissions attributable to missed opportunities of PMTCT services can be prevented by optimizing the uptake of PMTCT services. Identified risk factors for low PMTCT service uptake should be addressed through health facility and community-level interventions, including raising awareness, promoting women education, adolescent focused interventions, and strengthening linkages/referral-system between communities and health facilities.

Abstract Full-text [free] access
Editor’s notes: WHO recommends a comprehensive approach to prevention of mother-to-child transmission. This includes primary prevention of HIV among women of childbearing age, prevention of unintended pregnancies among women living with HIV, prevention of HIV transmission from a woman living with HIV to her infant and the provision of appropriate treatment, care and support to mothers living with HIV, their children and families.

This study assessed the uptake of antenatal and perinatal prevention of mother-to-child transmission services at four key stages along the prevention of mother-to-child transmission cascade (maternal HIV testing, CD4 count test/result, receiving maternal antiretroviral treatment and infant antiretroviral treatment).

Of all mothers included in the study, 31.7% were HIV-positive as identified by reactive infant antibody tests. Some 11% of HIV-positive mothers were reportedly unaware of their HIV-positive status. Being an adolescent was the strongest predictor of unawareness of HIV-positive status.

Overall 35% of mothers missed at least one step in the cascade. Dropout from the cascade, for all stages combined, accounted for 33.8% of HIV infections among infants, and maternal HIV status knowledge contributed to nearly half of this total.

The authors suggest that reported unawareness of being HIV-positive could be due to recent maternal infection or seroconversion during pregnancy. They call for improved repeat HIV testing during antenatal care and at delivery to identify new infections, and increased coverage of testing and counselling on safe sex for couples.

Interestingly the authors found that most pregnancies were unplanned (60%), demonstrating an important gap in the WHO prevention of mother-to-child transmission comprehensive strategy. Adolescent mothers (< 20 years) had a significantly higher rate of unplanned pregnancies compared to adult mothers. The authors suggest that programmes are necessary for sexually active adolescent girls to reduce both unplanned pregnancies and the risk of contracting HIV during conception or thereafter.

Integration of PMTCT and antenatal services improves combination antiretroviral therapy (cART) uptake for HIV-positive pregnant women in Southern Zambia - a prototype for option B+?


Background: Early initiation of combination anti-retroviral therapy (cART) for HIV-positive pregnant women can decrease vertical transmission to less than 5%. Programmatic barriers to early cART include decentralized care, disease stage assessment delays, and loss-to-follow-up.

Intervention: Our intervention had 3 components: integrated HIV and antenatal services in one location with one provider; lab courier to expedite CD4 counts; and community-based follow-up of women-infant pairs to improve PMTCT attendance. Pre-intervention HIV-positive pregnant women were referred to HIV clinics for disease stage assessment and cART initiation for advanced disease CD4< 350 or WHO stage >2.

Methods: We employed a quasi-experimental design with pre/post-intervention evaluations at 6 government antenatal clinics (ANC) in Southern Province, Zambia. Retrospective clinical data were collected from clinic registers during a 7-month baseline period. Post-intervention data were
collected from all ART-naive, HIV-positive pregnant women and their infants presenting to ANC from December 2011-June 2013.

Results: Data from 510 baseline women-infant pairs were analyzed and 624 pregnant women were enrolled during the intervention period. Proportion of HIV-positive pregnant women receiving CD4 counts increased from 50.6% to 77.2%, RR=1.81 95% CI: 1.57-2.08; p<0.01. Proportion of cART-eligible pregnant women initiated on cART increased from 27.5% to 71.5% RR=2.25, 95% CI: 1.78-2.83; p<0.01. Proportion of eligible HIV-exposed infants with documented 6-week HIV PCR test increased from 41.9% to 55.8%, RR=1.33, 95% CI: 1.18-1.51; p<0.01.

Conclusion: Integration of HIV care into ANC and community-based support improved uptake of CD4 counts, proportion of cART-eligible women initiated on cART and infants tested.

Abstract access

Editor’s notes: Integrating HIV services into other elements of health care, such as family planning or maternal health services, can increase uptake of HIV testing and antiretroviral therapy (ART) initiation. For pregnant women, timely HIV diagnosis and treatment can greatly reduce the probability of mother-to-child transmission. Integrating HIV services into maternal antenatal clinic (ANC) services therefore has potential to bring benefit to women living with HIV and their newborns. This paper describes an experimental study in which six ANC clinics in Zambia – all with high attendance and in provinces with high HIV prevalence – integrated HIV testing and treatment into their routine ANC services. This integration took the form of training existing ANC providers in HIV diagnosis and management; providing a rapid CD4 measurement service; and training volunteer lay counsellors to maintain regular contact with mothers living with HIV to improve ART initiation and adherence. The programme was associated with dramatic increases in ART initiation, early testing of infants and early ART initiation. The integrated approach used here has potential to improve prevention of mother-to-child transmission services. This is done through streamlined combination antiretroviral therapy (cART) initiation and decreasing time gaps in referral models. The approach assists in reducing HIV associated stigma and fear as the clinics offer maternal/child health services as well as HIV care. The clinics offer continuity through a community lay counsellor who follows the mother infant pair through pregnancy, delivery and breastfeeding. Further work is necessary to evaluate strategies for HIV care retention through similar models using community health workers and family-centric HIV care.

3. 15 million accessing treatment

Initiation of antiretroviral therapy in early asymptomatic HIV infection.


Background: Data from randomized trials are lacking on the benefits and risks of initiating antiretroviral therapy in patients with asymptomatic human immunodeficiency virus (HIV) infection who have a CD4+ count of more than 350 cells per cubic millimeter.

Methods: We randomly assigned HIV-positive adults who had a CD4+ count of more than 500 cells per cubic millimeter to start antiretroviral therapy immediately (immediate-initiation group) or to defer it until the CD4+ count decreased to 350 cells per cubic millimeter or until the development of the acquired immunodeficiency syndrome (AIDS) or another condition that
dictated the use of antiretroviral therapy (deferred-initiation group). The primary composite end point was any serious AIDS-related event, serious non-AIDS-related event, or death from any cause.

Results: A total of 4685 patients were followed for a mean of 3.0 years. At study entry, the median HIV viral load was 12 759 copies per milliliter, and the median CD4+ count was 651 cells per cubic millimeter. On May 15, 2015, on the basis of an interim analysis, the data and safety monitoring board determined that the study question had been answered and recommended that patients in the deferred-initiation group be offered antiretroviral therapy. The primary end point occurred in 42 patients in the immediate-initiation group (1.8%; 0.60 events per 100 person-years), as compared with 96 patients in the deferred-initiation group (4.1%; 1.38 events per 100 person-years), for a hazard ratio of 0.43 (95% confidence interval [CI], 0.30 to 0.62; P<0.001). Hazard ratios for serious AIDS-related and serious non-AIDS-related events were 0.28 (95% CI, 0.15 to 0.50; P<0.001) and 0.61 (95% CI, 0.38 to 0.97; P=0.04), respectively. More than two thirds of the primary end points (68%) occurred in patients with a CD4+ count of more than 500 cells per cubic millimeter. The risks of a grade 4 event were similar in the two groups, as were the risks of unscheduled hospital admissions.

Conclusions: The initiation of antiretroviral therapy in HIV-positive adults with a CD4+ count of more than 500 cells per cubic millimeter provided net benefits over starting such therapy in patients after the CD4+ count had declined to 350 cells per cubic millimeter.

Abstract Full-text [free] access

Editor’s notes: Guidelines on when to start antiretroviral therapy (ART) are rapidly evolving. The major point of uncertainty, and disagreement between guidelines, has been whether the benefits to individuals of starting ART outweigh the risks for people with high CD4 counts, where the absolute risk of morbidity and mortality is relatively low.

The START study addressed this question among people with CD4 counts greater than 500 cells per μl. Study participants were recruited across the global regions, with the largest number from Europe (33%) followed by Latin America (25%) and Africa (21%). Some 55% were gay men and other men who have sex with men. Retention in the study was very good, and virologic outcomes among people who started ART were excellent (98% and 97% had virologic suppression by 12 months in the immediate versus deferred study arms). There was a 57% reduction in the hazard of the primary outcome, a composite of serious AIDS-associated events, serious non-AIDS associated events or death from any cause. The most common AIDS-associated events were tuberculosis (mostly seen in African participants), malignant lymphoma and Kaposi’s sarcoma. Among the serious non-AIDS events, cancers unrelated to AIDS were reduced by 50%, but interestingly there was no change in cardiovascular events. There was no increase in risk of serious adverse events. Interestingly the magnitude of risk reduction for the primary outcome was similar in high- and low-income countries.

These results will be very important as ART guidelines are reviewed and are likely to lead to recommendations for ART initiation, regardless of CD4 count in most settings. The authors note that, with a relatively low absolute risk of serious events, some people with high CD4 counts may opt to defer treatment, and this trial has produced very useful data to inform this discussion. Benefits from earlier ART initiation are dependent on earlier testing. With an estimated 50% of people with HIV globally unaware of their status, the uptake of testing by asymptomatic people will need to be increased. In addition, retention in care will need to be optimised if the potential benefits of ART demonstrated by this study are to be realised.
Single-dose nevirapine exposure does not affect response to antiretroviral therapy in HIV-infected African children aged below 3 years.


Objectives: To assess the impact of exposure to single-dose nevirapine (sdNVP) on virological response in young Ugandan/Zimbabwean children (<3 years) initiating antiretroviral therapy (ART), and to investigate other predictors of response.

Design: Observational analysis within the ARROW randomized trial.

Methods: sdNVP exposure was ascertained by the caregiver’s self-report when the child initiated non-nucleoside reverse transcriptase inhibitor (NNRTI)-based ART. Viral load was assayed retrospectively over a median 4.1 years of follow-up. Multivariable logistic regression models were used to identify independent predictors of viral load below 80 copies/ml, 48 and 144 weeks after ART initiation (backwards elimination, exit P = 0.1).

Results: Median (IQR) age at ART initiation was 17 (10-23) months in 78 sdNVP-exposed children vs. 21 (14-27) months in 289 non-exposed children (36 vs. 20% <12 months). At week 48, 49 of 73 (67%) sdNVP-exposed and 154 of 272 (57%) non-exposed children had viral load below 80 copies/ml [adjusted odds ratio (aOR) 2.34 (1.26-4.34), P = 0.007]; 79 and 77% had viral load below 400 copies/ml. Suppression was significantly lower in males (P = 0.009), those with higher pre-ART viral load (P = 0.001), taking syrups (P = 0.05) and with lower self-reported adherence (P = 0.04). At week 144, 55 of 73 (75%) exposed and 188 of 272 (69%) non-exposed children had less than 80 copies/ml [aOR 1.75 (0.93-3.29), P = 0.08]. There was no difference between children with and without previous sdNVP exposure in intermediate/high-level resistance to NRTIs (P > 0.3) or NNRTIs (P > 0.1) (n = 88) at week 144.

Conclusion: Given the limited global availability of lopinavir/ritonavir, its significant formulation challenges in young children, and the significant paediatric treatment gap, tablet fixed-dose-combination NVP-based ART remains a good alternative to syrup lopinavir-based ART for children, particularly those over 1 year and even if exposed to sdNVP.

Abstract access

Editor’s notes: Universal initiation of antiretroviral therapy (ART) is recommended for all children below the age of five years, regardless of immune or clinical status. World Health Organization recommends initiation with lopinavir/ritonavir-containing ART in children aged below three years. This was prompted by the P1060 trials which showed a poorer virologic response to nevirapine compared to lopinavir-containing regimens among infants exposed and unexposed, to single-dose nevirapine (sd NVP) as prophylaxis against mother-to-child HIV transmission. Previous studies had shown a poorer response to nevirapine-containing combination antiretroviral therapy (ART) subsequently initiated by mothers exposed to sd NVP.

However, lopinavir/ritonavir for young children is only available as a liquid formulation. This has limited availability, is highly unpalatable, has cold chain requirements and is bulky and conspicuous to transport. Where lopinavir-containing ART is not feasible, guidelines suggest non-nucleoside reverse transcriptase inhibitor (NNRTI)-based regimens as an alternative. The NNRTI of choice is nevirapine, because dosing of efavirenz is problematic in young children. Understanding whether sd NVP is associated with substantially greater risks of virologic failure in children who start nevirapine containing regimens is therefore important.
This study compared the risk of virologic failure in young children (aged between six months and three years) initiating nevirapine-containing ART who had been exposed to single dose NVP, compared to people who had not. The study found no higher risk of virologic failure in people who had been exposed to sd NVP compared to people who had not, either at 48 or at 144 weeks after ART initiation. This remained true regardless of whether viral-load cut-off of 80, 400 or 1000 copies/ml was used to define virologic failure. Furthermore, there was no difference between children with and without sd NVP exposure in the percentage of clinically-significant NRTI or NNRTI resistance mutations.

As expected, a high pre-ART viral load was a strong predictor of poor virologic response. Importantly, receiving ART with syrup compared to tablets also predicted poor virologic response, and was equivalent to initiating ART with a 1 log_{10} higher viral load. This is a similar magnitude of difference in virologic response as that seen between lopinavir- versus nevirapine- containing regimens in the P1060 trials. As triple-drug nevirapine-based tablets are available for young children, this would imply that a tablet nevirapine-based regimen may have similar virologic response to a syrup lopinavir-based regimen in young children.

The study did not do a randomised comparison and sd NVP exposure was based on self-report. Also, a third of the participants took NNRTI for 36 weeks only, following which they were switched to triple NRTI regimens. However, the results were similar when the analyses were restricted to people who took NNRTI-based regimens throughout the study period.

This study should provide reassurance to healthcare providers in resource-limited settings that nevirapine-based ART is a good alternative to syrup lopinavir-based ART, even when there is prior exposure to sd NVP.

A randomised controlled trial of real-time electronic adherence monitoring with text message dosing reminders in people starting first-line antiretroviral therapy.


Background: There are conflicting findings about whether mobile phone text message reminders impact on antiretroviral adherence. We hypothesized that text reminders sent when dosing was late would improve adherence and HIV viral suppression.

Methods: ART-naive participants, from a South African outpatient ART clinic, were randomised to standard of care (SoC, three pre-treatment education sessions), or intervention (SoC and automated text reminders if dosing >30 minutes late). Dosing time was recorded by real-time electronic adherence monitoring devices (EAMD), given to participants at ART start. CD4 cell count and HIV RNA were determined at baseline, 16 and 48 weeks. Primary outcome was cumulative adherence execution by EAMD. HIV-1 viral suppression (<40 copies/ml) at week 48 and count of treatment interruptions (TIs) >72 hours were secondary outcomes. Analysis was by intention to treat (missing=failure). Registration was with the Pan-African Clinical Trials Registry: PACTR201311000641402.

Results: 230 participants were randomly assigned to control (n=115) or intervention (n=115) arms. Median adherence was 82.1% (IQR 56.6-94.6%) in the intervention arm, compared to 80.4% (IQR 52.8-93.8%) for SoC (adjusted odds ratio (aOR) for adherence 1.08, 95%CI:0.77-1.52). Suppressed HIV RNA (<40 copies/ml) occurred in 80 (69.6%) of control and 75 (65.2%) of intervention; aOR for virological failure in intervention arm 0.77, 95%CI:0.42-1.40). In the
intervention arm the count of TIs of >72hours was reduced (adjusted incident rate ratio 0.84, 95%CI:0.75-0.94).

Conclusion: Text message reminders linked to late doses detected by real-time adherence monitoring reduced the number of prolonged treatment interruptions, but did not significantly improve adherence or viral suppression.

Abstract access

Editor’s notes: Maximising adherence to treatment is a key issue for management of chronic disease. In the case of antiretroviral therapy (ART), good adherence is essential not only to optimise treatment outcomes for the individual but also to minimise the emergence of drug-resistant disease. Electronic adherence monitoring devices (EAMD) have been used as a research tool but have been too expensive for routine use. However lower-cost devices are being developed with potential for wider use, and would be very valuable if they are shown to improve treatment outcomes.

In this small trial from Cape Town, South Africa, adults initiating ART were randomised either to receive an EAMD as a simple pillbox, recording box opening but without any reminder function, or an EAMD which sent a text message reminder if the box was not opened within 30 minutes of the scheduled dosing time. This time window for the reminder was selected by study participants, who were mostly taking ART as a single evening dose.

There was no difference in adherence by study arm or in virologic suppression. As might be expected, adherence based on self-reported three-day recall or pill count was higher (median 100% in both arms for both measures) compared to adherence measured by EAMD (82.1% in programme and 80.4% in the control arm, calculated as number of days the device was opened divided by the number of days in care). However in the programme arm there were fewer treatment interruptions exceeding 72 hours, relevant to the risk of developing resistance on a non-nucleoside reverse-transcriptase inhibitors (NNRTI)-based regimen. The authors point out that treatment adherence at this clinic is generally very good, attributed to strong adherence support provided by the clinic, which could have contributed to the negative result.

This study suggests that dose reminders alone are unlikely to improve adherence to ART, which is not surprising given the complexity of adherence behaviours. Further work needs to explore whether other activities based on EAMDS will perform better than text message reminders alone.

Monitoring and switching of first-line antiretroviral therapy in sub-Saharan Africa: collaborative analysis of adult treatment cohorts.


Background: HIV-1 viral load testing is recommended to monitor antiretroviral therapy (ART) but is not universally available. The aim of our study was to assess monitoring of first-line ART and switching to second-line ART in sub-Saharan Africa.

Methods: We did a collaborative analysis of cohort studies from 16 countries in east Africa, southern Africa, and west Africa that participate in the international epidemiological database to evaluate AIDS (IeDEA). We included adults infected with HIV-1 who started combination ART between January, 2004, and January, 2013. We defined switching of ART as a change from a non-
nucleoside reverse-transcriptase inhibitor (NNRTI)-based regimen to one including a protease inhibitor, with adjustment of one or more nucleoside reverse-transcriptase inhibitors (NRTIs). Virological and immunological failures were defined according to WHO criteria. We calculated cumulative probabilities of switching and hazard ratios with 95% CIs comparing routine viral load monitoring, targeted viral load monitoring, CD4 monitoring, and clinical monitoring, adjusting for programme and individual characteristics. 

Findings: Of 297 825 eligible patients, 10 352 (3%) switched to second-line ART during 782 412 person-years of follow-up. Compared with CD4 monitoring, hazard ratios for switching were 3·15 (95% CI 2·92–3·40) for routine viral load monitoring, 1·21 (1·13–1·30) for targeted viral load monitoring, and 0·49 (0·43–0·56) for clinical monitoring. Of 6450 patients with confirmed virological failure, 58·0% (95% CI 56·5–59·6) switched by 2 years, and of 15 892 patients with confirmed immunological failure, 19·3% (18·5–20·0) switched by 2 years. Of 10 352 patients who switched, evidence of treatment failure based on one CD4 count or viral load measurement ranged from 86 (32%) of 268 patients with clinical monitoring to 3754 (84%) of 4452 with targeted viral load monitoring. Median CD4 counts at switching were 215 cells per μL (IQR 117–335) with routine viral load monitoring, but were lower with other types of monitoring (range 114–133 cells per μL).

Interpretation: Overall, few patients switched to second-line ART and switching happened late in the absence of routine viral load monitoring. Switching was more common and happened earlier after initiation of ART with targeted or routine viral load testing.

Abstract access

**Editor’s notes:** Routine viral load monitoring should allow the early identification of first-line antiretroviral therapy (ART) failure, allowing prompt switch to second-line ART. Prolongation of treatment with a failing regimen compromises future therapeutic options (through the accumulation of drug resistance mutations) and potentially leads to increased morbidity and mortality. Previous reports from Africa have suggested that surprisingly few people switch to second-line therapy, even in programmes with routine viral load monitoring. This raises concerns that there are challenges on the ground with identification and management of ART failure.

This is a comprehensive analysis bringing together data from a number of well-characterised cohorts in Africa. In this analysis, switching to second-line ART was rare (3% over an average of almost three years follow-up). In programmes with routine viral load monitoring, only half of the people with confirmed virologic failure on first-line ART (two viral loads >1000 copies/ml) were recorded as having been switched to second-line ART. Furthermore, half of the people that were switched to a second-line regimen did not have evidence of confirmed virologic failure, suggesting that some may have been switched too early without first attempting adherence programmes which may achieve re-suppression on first-line ART. Unsurprisingly, rates of switching were lower in programmes with CD4+ monitoring (with or without targeted viral load testing) or clinical monitoring alone.

While guidelines and algorithms around identification and management of first-line ART failure are relatively clear and straightforward, translating this into action on the ground seems to be difficult. At least part of this is likely to be due to the lack of tools to reliably measure adherence and the consequent difficulty that frontline health care workers have in identifying people that truly require a switch to second-line ART. Moreover, most programmes still do not routinely monitor indicators relating to virologic suppression or treatment failure and so this might not be seen as a priority by health care workers and programme managers. There is a need for research to explore how best to maximise virologic suppression in resource-constrained settings, as well as studies to evaluate the impact of programmes such as point-of-care viral load testing.
4. Avoid TB deaths

A trial of early antiretrovirals and isoniazid preventive therapy in Africa.


Background: In sub-Saharan Africa, the burden of human immunodeficiency virus (HIV)-associated tuberculosis is high. We conducted a trial with a 2-by-2 factorial design to assess the benefits of early antiretroviral therapy (ART), 6-month isoniazid preventive therapy (IPT), or both among HIV-infected adults with high CD4+ cell counts in Ivory Coast.

Methods: We included participants who had HIV type 1 infection and a CD4+ count of less than 800 cells per cubic millimeter and who met no criteria for starting ART according to World Health Organization (WHO) guidelines. Participants were randomly assigned to one of four treatment groups: deferred ART (ART initiation according to WHO criteria), deferred ART plus IPT, early ART (immediate ART initiation), or early ART plus IPT. The primary end point was a composite of diseases included in the case definition of the acquired immunodeficiency syndrome (AIDS), non-AIDS-defining cancer, non-AIDS-defining invasive bacterial disease, or death from any cause at 30 months. We used Cox proportional models to compare outcomes between the deferred-ART and early-ART strategies and between the IPT and no-IPT strategies.

Results: A total of 2056 patients (41% with a baseline CD4+ count of ≥500 cells per cubic millimeter) were followed for 4757 patient-years. A total of 204 primary end-point events were observed (3.8 events per 100 person-years; 95% confidence interval [CI], 3.3 to 4.4), including 68 in patients with a baseline CD4+ count of at least 500 cells per cubic millimeter (3.2 events per 100 person-years; 95% CI, 2.4 to 4.0). Tuberculosis and invasive bacterial diseases accounted for 42% and 27% of primary end-point events, respectively. The risk of death or severe HIV-related illness was lower with early ART than with deferred ART (adjusted hazard ratio, 0.56; 95% CI, 0.41 to 0.76; adjusted hazard ratio among patients with a baseline CD4+ count of ≥500 cells per cubic millimeter, 0.56; 95% CI, 0.33 to 0.94) and lower with IPT than with no IPT (adjusted hazard ratio, 0.65; 95% CI, 0.48 to 0.88; adjusted hazard ratio among patients with a baseline CD4+ count of ≥500 cells per cubic millimeter, 0.61; 95% CI, 0.36 to 1.01). The 30-month probability of grade 3 or 4 adverse events did not differ significantly among the strategies.

Conclusions: In this African country, immediate ART and 6 months of IPT independently led to lower rates of severe illness than did deferred ART and no IPT, both overall and among patients with CD4+ counts of at least 500 cells per cubic millimeter.

Abstract Full-text [free] access

Editor’s notes: Recommendations and guidelines on the optimal time to start antiretroviral therapy (ART) are evolving rapidly. These are driven by improved ART regimens with better safety profiles, the desire to improve further the survival and health of people living with HIV, and the need to halt HIV transmission. The TEMPRANO study in Côte d’Ivoire is among several randomised trials reporting significant benefits in severe morbidity and mortality from early ART initiation, before serious decline in CD4 count or presentation with clinical disease. Findings are consistent with the multi-site START trial (also discussed in this edition of HIV This Month) and long-term follow-up from HPTN 052 (a trial of early ART among HIV serodiscordant couples), despite the different CD4 count cut-offs, outcome definitions etc. Collectively these findings were a major focus of discussion at the International AIDS Society conference in Vancouver, Canada in July 2015, and they will shape ongoing revision of the WHO treatment guidelines.
The TEMPRANO study looked at immediate ART (usually tenofovir-emtricitabine + efavirenz) plus or minus six months of isoniazid prophylaxis in people who did not meet the (evolving) WHO criteria for eligibility, in a rigorous, controlled trial with a 2x2 factorial design. The results illustrate significant reductions in risk of a serious event (TB or HIV-associated illness) or death attributable to both programmes over 30 months. Tuberculosis represented 42% of all primary endpoints. It should be noted that the absolute risk of serious events (TB or severe illness or death) was low in the group with higher baseline CD4 counts.

Early ART initiation will be required to meet the UNAIDS target of 90-90-90 (90% of HIV positive individuals knowing their status, 90% of people being on ART and 90% of people on ART being virally suppressed), but may only have an impact on the second of these targets. Observers recognise that the challenge of earlier diagnosis, and retention and adherence on treatment, remain barriers to maximising public health impact of the very promising results of early treatment trials.

In the TEMPRANO study a significant proportion of people screened for this study declined to participate and there was a further loss to follow-up during the study, proportions which may increase in an operational setting. There was a higher rate of short term adverse events in the earlier treatment group, relating to the toxicity of the drugs themselves.

The evidence for earlier ART in terms of individual benefit and reduction of transmission is increasing, particularly in settings with high burdens of tuberculosis and bacterial disease. The challenge will be engaging populations of healthy people and designing treatment systems and strategies to optimise that engagement. Long term follow-up of the cohorts in these trials will be informative as will trials of treatment delivery strategies.

Incidence of tuberculosis among young children in rural Mozambique.


Background: Tuberculosis (TB) contributes significantly to child morbidity and mortality. This study aimed to estimate the minimum community-based incidence rate of TB among children <3 years of age in Southern Mozambique.

Methods: Between October 2011 and October 2012, in the Manhica District Health and Demographic Surveillance System, we enrolled prospectively all presumptive TB cases younger than 3 years of age through passive and active case finding. Participants included all children who were either symptomatic or were close contacts of a notified adult smear-positive pulmonary TB. Children were clinically evaluated at baseline and follow-up visits. Investigation for TB disease included chest radiography, HIV and tuberculin skin testing as well as gastric aspirate and induced sputum sampling, which were processed for smear, culture and mycobacterial molecular identification.

Results: During the study period, 13 764 children <3 years contributed to a total of 9575 person-years. Out of the 789 presumptive TB cases enrolled, 13 had TB culture confirmation and 32 were probable TB cases. The minimum community-based incidence rate of TB (confirmed plus probable cases) was 470 of 100 000 person-years (95% confidence interval: 343-629 of 100 000). HIV co-infection was present in 44% of the TB cases.

Conclusion: These data highlight the huge burden of pediatric TB. This study provides one of the first prospective population-based incidence data of childhood tuberculosis and adds valuable
information to the global effort of producing better estimates, a critical step to inform public health policy.

Abstract access

Editor’s notes: Mozambique is one of the few high HIV/TB burden countries where TB prevalence and incidence has not improved in recent years. This prospective cohort study nested within a rural demographic surveillance site brings to light the immense burden of paediatric tuberculosis in the southern part of the country. The findings of an estimated minimum community-based TB incidence rate in children aged < 3 years of 470 per 100 000 person years (nearly double the number of cases notified) emphasise the gross under-detection of paediatric tuberculosis in this region.

Children are unlikely to contribute to onward transmission of Mycobacterium tuberculosis (Mt) because they rarely have large numbers of bacilli in respiratory secretions. Thus, from a public health point of view, childhood tuberculosis has not until recently been considered a priority in high burden settings. One of the study’s strengths is the huge effort made to confirm TB diagnoses, which, due to low numbers of bacilli in sputum and inability to produce sputum samples, is notoriously difficult in young children. Accurate estimates of paediatric TB (especially in the very young, e.g. ≤3 years), as attempted by this population-based study, act as a critical indicator of the effectiveness of programmes to curtail community transmission. These findings therefore signal an extremely high level of on-going Mt transmission and the urgent need for effective public health programmes to halt the TB/HIV epidemic in Mozambique.

5. Close the resource gap

Shamba Maisha: randomized controlled trial of an agricultural and finance intervention to improve HIV health outcomes in Kenya.


Objectives: Food insecurity and HIV/AIDS outcomes are inextricably linked in sub-Saharan Africa. We report on health and nutritional outcomes of a multisectoral agricultural intervention trial among HIV-infected adults in rural Kenya.

Design: This is a pilot cluster randomized controlled trial.

Methods: The intervention included a human-powered water pump, a microfinance loan to purchase farm commodities, and education in sustainable farming practices and financial management. Two health facilities in Nyanza Region, Kenya were randomly assigned as intervention or control. HIV-infected adults 18 to 49 years old who were on antiretroviral therapy and had access to surface water and land were enrolled beginning in April 2012 and followed quarterly for 1 year. Data were collected on nutritional parameters, CD4 T-lymphocyte counts, and HIV RNA. Differences in fixed-effects regression models were used to test whether patterns in health outcomes differed over time from baseline between the intervention and control arms.

Results: We enrolled 72 and 68 participants in the intervention and control groups, respectively. At 12 months follow-up, we found a statistically significant increase in CD4 cell counts (165 cells/µl, P < 0.001) and proportion virologically suppressed in the intervention arm compared with the control arm (comparative improvement in proportion of 0.33 suppressed, odds ratio 7.6, 95% confidence interval: 2.2-26.8). Intervention participants experienced significant improvements in
food security (3.6 scale points higher, $P < 0.001$) and frequency of food consumption (9.4 times per week greater frequency, $P = 0.013$) compared to controls.

Conclusion: Livelihood interventions may be a promising approach to tackle the intersecting problems of food insecurity, poverty and HIV/AIDS morbidity.

Abstract access

Editor’s notes: There is compelling evidence of a vicious cycle between food insecurity and HIV transmission, morbidity and mortality. Studies have been finding alarmingly high rates of moderate and severe food insecurity among ART initiates in east Africa, at least 70%. At a time when the world is aiming to achieve the 90-90-90 targets, (90% of HIV positive individuals knowing their status, 90% of people being on ART and 90% of people on ART being virally suppressed) and thus increase viral suppression to 90%, among people on antiretroviral therapy, it is clear that the effectiveness and efficiency of treatment will depend on how food insecurity is addressed, within and/or alongside the HIV programme.

In this pilot study in Kenya, the authors report on an agricultural and microfinance programme provided to food-insecure adults living with HIV, who had access to farming land and surface water. Study participants were mainly established patients who had been on ART for an average of 2.8 years. The study finds a significant increase in CD4 cell counts (165 cells/mm$^3$) and a comparative increase in the proportion of patients with virologic suppression, of 33%. In addition, significant improvements were found on the food security scale. These included the diversity and frequency of food consumption, as well as increases in BMI, despite no significant changes in food expenditures. However, it is important to note that the programme and control samples were unbalanced, with the programme group starting with higher food insecurity and a lower proportion of virologic suppression. Moreover, with only two sites, the study could not separate the programme effects from cluster-level variables, underscoring the need for a larger cluster RCT to confirm these findings.

Although this is a pilot RCT with a small sample size and other limitations, it provides promising evidence that a multi-sectoral agricultural and microfinance programme can have direct effects on ART outcomes, as well as impacting on food insecurity and nutrition outcome measures. While previous studies have reported on the effects of food assistance for people on ART, this study is an important addition to the evidence, as it is one of the first to report on a potentially sustainable agricultural-microfinance programme. Also, by measuring multiple outcomes across sectors, it allows for a more balanced appraisal of the programmes societal benefits, rather than only considering its HIV dividend.

6. Eliminate stigma and discrimination

The immediate effect of the Same-Sex Marriage Prohibition Act on stigma, discrimination, and engagement on HIV prevention and treatment services in men who have sex with men in Nigeria: analysis of prospective data from the TRUST cohort.


Background: In January, 2014, the Same-Sex Marriage Prohibition Act was signed into law in Nigeria, further criminalising same-sex sexual relationships. We aimed to assess the immediate effect of this prohibition act on stigma, discrimination, and engagement in HIV prevention and treatment services in men who have sex with men (MSM) in Nigeria.
Methods: The TRUST cohort study uses respondent-driven sampling to assess the feasibility and effectiveness of engagement of MSM in HIV prevention and treatment services at a clinical site located with a community-based organisation trusted by the MSM community. **TRUST is a prospective implementation research cohort of MSM (≥16 years) in Abuja, Nigeria.** We compared HIV clinical outcomes and stigma, including fear and avoidance of health care, across baseline and quarterly visits before and after implementation of the Same-Sex Marriage Prohibition Act. Outcomes assessed were measures of stigma and discrimination, loss to follow-up, antiretroviral therapy status, and viral load. We compared outcomes before and after the legislation with chi² statistics, and estimated incident stigma-related events and loss to follow-up with Poisson regression.

Findings: Between March 19, 2013, and Aug 7, 2014, 707 MSM participated in baseline study procedures, contributing to 756 before legislation (prelaw) and 420 after legislation (postlaw) visits. **Reported history of fear of seeking health care was significantly higher in postlaw visits than in prelaw visits (n=161 [38%] vs n=187 [25%]; p<0.0001), as was avoidance of health care (n=118 [28%] vs n=151 [20%]; p=0.001).** In incidence analyses, of 192 MSM with follow-up data and no history of an event at baseline, **reported fear of seeking health care was higher in the postlaw than the prelaw period (n=144; incidence rate ratio 2.57, 95% CI 1.29-5.10; p=0.007); loss to follow-up and incident healthcare avoidance were similar across periods.** Of the 161 (89%) of 181 HIV-infected MSM with HIV viral loads available, those who had disclosed sexual behaviour with a health-care provider were more often virally suppressed at baseline than those with no previous disclosure (18 [29%] of 62 vs 13 [13%] of 99 men; p=0.013).

Interpretation: These analyses represent individual-level, quantitative, real-time prospective data for the health-related effects resulting from the enactment of legislation further criminalising same-sex practices. The negative effects of HIV treatment and care in MSM reinforce the unintended consequences of such legislation on global goals of HIV eradication. Strategies to reach MSM less likely to engage in HIV testing and care in highly stigmatised environments are needed to reduce time to HIV diagnosis and treatment.

**Abstract access**

**Editor’s notes:** Despite the recent implementation of progressive laws on same-sex relationships and marriage in several settings, other countries – including Nigeria – have moved to criminalise same-sex practises. As well as broader human rights concerns, there is the risk that policies that criminalise same-sex practices, or the community groups addressing the health-related needs of these populations, might restrict the coverage of HIV prevention, treatment and care programmes. However, despite these concerns, there is extremely limited quantitative evidence on the impact of such policies. In Nigeria, the Same-Sex Marriage Prohibition Act was passed in 2011, coming into law in 2014. Before this legislation, consensual sex between male same-sex couples was already prohibited. The new law further criminalised same sex practices, including prohibiting participation in organisations and service provision. This study opportunistically analysed data from an on-going prospective cohort study of gay men and other men who have sex with men in Abuja, which had started prior to the law’s implementation, and continued after its introduction. The study assessed the degree to which this legislation impacted on gay men and other men who have sex with men’s fear and health service use. Unsurprisingly, perhaps, the study illustrates that the law did impact negatively on gay men and other men who have sex with men – significantly increasing their fear of and avoidance of health services, as well as increasing their levels of harassment and experience of blackmail. Prior to the new legislation, levels were already high, with the new law seeming to exacerbate existing barriers and stigma. The findings are important, illustrating how regressive laws...
can increase the stigmatisation of already marginalised groups, and undermine the gay men and other men who have sex with men’s access to health associated services. Supportive policy environments, along with HIV programmes for marginalised populations, form an essential part of an effective HIV response.

7. Strengthening HIV integration

Going beyond the vertical: leveraging a national HIV quality improvement programme to address other health priorities in Haiti.


Although the central role of quality to achieve targeted population health goals is widely recognized, how to spread the capacity to measure and improve quality across programmes has not been widely studied. We describe the successful leveraging of expertise and framework of a national HIV quality improvement programme to spread capacity and improve quality across a network of clinics in HIV and other targeted areas of healthcare delivery in rural Haiti. The work was led by Zamni LaSante, a Haitian nongovernment organization and its sister organization, Partners In Health working in partnership with the Haitian Ministry of Health in the Plateau Central and Lower Artibonite regions in 12 public sector facilities. Data included routinely collected organizational assessments of facility quality improvement capacity, national HIV performance measures and Zamni LaSante programme records. We found that facility quality improvement capacity increased with spread from HIV to other areas of inpatient and outpatient care, including tuberculosis (TB), maternal health and inpatient services in all 12 supported healthcare facilities. A significant increase in the quality of HIV care was also seen in most areas, including CD4 monitoring, TB screening, HIV treatment (all P < 0.01) and nutritional assessment and prevention of mother-to-child transmission (both P < .05), with an increase in average facility performance from 39 to 72% (P < .01). In conclusion, using a diagonal approach to leverage a national vertical programme for wider benefit resulted in accelerated change in professional culture and increased capacity to spread quality improvement activities across facilities and areas of healthcare delivery. This led to improvement within and beyond HIV care and contributed to the goal of quality of care for all.

Abstract access

Editor’s notes: With the current changing HIV-funding landscape, there is increased interest in leveraging disease-specific programmes using a ‘diagonal approach’ to achieve a broader health systems goal. This paper describes a good example of leveraging an HIV-specific quality improvement framework to realise multiple benefits. The authors describe a quality improvement programme which was implemented across 12 health facilities in Haiti. Although the programme was initially HIV-specific, it was expanded to other disease areas including family planning, TB screening and management of heart failure. The spread to other disease areas was facilitated by the programme’s focus on capacity building, resulting in strengthened leadership and ownership across the sites. This paper is a great example of the potential for a ‘diagonal approach’ to maximise system-wide benefits within the context of a vertical programme.

Alcohol use, partner violence, and depression: a cluster randomized controlled trial among urban South African mothers over 3 years.
Introduction: Pregnant South African women with histories of drinking alcohol, abuse by violent partners, depression, and living with HIV are likely to have their post-birth trajectories over 36 months significantly influenced by these risks.

Design: All pregnant women in 24 Cape Town neighborhoods were recruited into a cluster RCT by neighborhood to either: (1) a standard care condition (n=12 neighborhoods, n=594 mothers); or (2) a home-visiting intervention condition (n=12 neighborhoods, n=644 mothers).

Setting/participants: Pregnant women residing in urban, low-income neighborhoods in Cape Town, South Africa.

Intervention: Home visiting included prenatal and postnatal visits by community health workers (Mentor Mothers) focusing on general maternal and child health, HIV/tuberculosis, alcohol use, and nutrition.

Main outcome measures: Mothers were assessed in pregnancy and at 18 and 36 months post birth: 80.6% of mothers completed all assessments between 2009 and 2014 and were included in these analyses performed in 2014. Longitudinal structural equation modeling examined alcohol use, partner violence, and depression at the baseline and 18-month interviews as predictors of maternal outcomes at 36 months post birth.

Results: Relative to standard care, intervention mothers were significantly less likely to report depressive symptoms and more positive quality of life at 36 months. Alcohol use was significantly related to use over time, but was also related to depression and HIV status at each assessment and partner violence at 36 months.

Conclusions: Alcohol, partner violence, and depression are significantly related over time. A home-visiting intervention improved the emotional health of low-income mothers even when depression was not initially targeted.

Abstract  Full-text [free] access

Editor’s notes: This study evaluates the use of community health workers (CHW) to implement a programme to improve maternal wellbeing among low-income mothers in Cape Town, South Africa from pregnancy until 36 months after birth. This is a setting with high prevalence of HIV (about 30% of pregnant women are HIV positive in the Western Cape), and the programme followed a behaviour-change model focused on alcohol and HIV (but not intimate partner violence [IPV] or depression). The programme was associated with improved maternal emotional health at 36 months. However, there was relatively little change in alcohol use or IPV. Overall, the study underlines the inter-relationships between alcohol use, intimate partner violence, HIV and depression. Further, it suggests that future programmes should train CHWs to expand their activities to depression and IPV as well as HIV, and alcohol.