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

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   - Measuring adherence – a promising approach with caregivers of children living with HIV
   - Only a quarter of people living with HIV in South Africa virally suppressed
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• Psychological distress and HIV after financial meltdown in Zimbabwe

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Peter Godfrey-Faussett and Celeste Sandoval
UNAIDS
1. HIV testing and treatment

Factors that motivated otherwise healthy HIV-positive young adults to access HIV testing and treatment in South Africa.


The World Health Organization recommends early initiation of HIV antiretroviral therapy (ART) for all those infected with the virus at any CD4 count. Successfully reaching individuals with relatively high CD4 counts depends in large part on healthy individuals seeking testing and treatment; however, little is known about factors motivating this decision. We conducted a qualitative study to explore this issue among 25 young HIV-positive adults (age 18-35) with a CD4 count >350 cells/mm$^3$ who recently started or made the decision to start ART in Gugulethu, South Africa. Using an inductive content analytical approach, we found that most individuals sought testing and treatment early in the disease progression because of a desire to appear healthy thereby avoiding stigma associated with AIDS. Other factors included social support, responsibilities and aspirations, normalcy of having HIV, and accessible services. These findings suggest that maintenance of physical appearance should be included in the development of novel testing and treatment interventions.

Abstract access

Editor’s notes: A lot has been written on why people delay entry into care, when they are living with HIV. The guidance that all people living with HIV should now start treatment means that many people who are healthy are being offered treatment. The authors of this paper found that in a small sample of people in South Africa, looking healthy mattered. There was a value in the message that ART could maintain health, and in the words of one participant in their study, to ‘remain beautiful’. In addition, other positive anticipated results of taking ART emerged from the data. Young people saw the benefit in maintaining their health so they can help their family in the future, for example. However, despite the positive messages on appearance and a future role for the family and society, many concerns remained. Participants wanted privacy to live with HIV without others knowing. Fears of stigma, fears of an altered appearance and faltering strength haunted participants. The authors stress the value of the positive messaging of ART as an aid to sustaining a healthy appearance. They suggest that this messaging could be used to encourage people to start ART promptly.

Improved adherence to antiretroviral therapy observed among HIV-infected children whose caregivers had positive beliefs in medicine in sub-Saharan Africa.


A high level of adherence to antiretroviral treatment is essential for optimal clinical outcomes in HIV infection, but measuring adherence is difficult. We investigated whether responses to a questionnaire eliciting caregiver beliefs in medicines were associated with adherence of their child (median age 2.8 years), and whether this in turn was associated with viral suppression. We used the validated beliefs in medicine questionnaire (BMQ) to measure caregiver beliefs, and medication event monitoring system caps to measure adherence. We found significant associations between BMQ scores and adherence, and between adherence and viral suppression.
Among children initiating antiretroviral therapy (ART), we also found significant associations between BMQ 'necessity' scores, and BMQ 'necessity-concerns' scores, and later viral suppression. This suggests that the BMQ may be a valuable tool when used alongside other adherence measures, and that it remains important to keep caregivers well informed about the long-term necessity of their child’s ART.

Abstract

Editor’s notes: How we measure adherence to antiretroviral therapy has long been a challenge within HIV clinical care. We need to know who is struggling with their HIV treatment so that we can provide support to improve their treatment taking behaviour before treatment resistance and other complex clinical problems take hold. This can be an especially relevant concern for children who will need to take HIV treatment throughout their lives. The analysis within this paper proffers a relatively accessible means to identify families who are more likely to encounter adherence problems. This potentially allows people to receive pre-emptive support before clinical problems arise.

The authors tested their hypothesis that the children of caregivers who had concerns about the overuse and associated toxicity of medicine and/or had strong beliefs in divine intervention as curative, relative to their belief in the necessity of medicines, would be less likely to be virally suppressed. Such beliefs were measured in a validated ‘belief in medicine’ questionnaire. Although this was used within a clinical trial setting it is potentially simple enough to feasibly be used in more general clinical settings. This measure could identify particular ‘at-risk’ caregiver groups to inform not only the provision of tailored adherence support but also at which critical time points such support should be delivered.

The continuum of HIV care in South Africa: implications for achieving the second and third UNAIDS 90-90-90 targets.


Background: We characterize engagement with HIV care in South Africa in 2012 to identify areas for improvement towards achieving global 90-90-90 targets.

Methods: Over 3.9 million CD4 cell count and 2.7 million viral load measurements reported in 2012 in the public sector were extracted from the national laboratory electronic database. The number of persons living with HIV (PLHIV), number and proportion in HIV care, on antiretroviral therapy (ART) and with viral suppression (viral load <400 copies/ml) were estimated and stratified by sex and age group. Modified Poisson regression approach was used to examine associations between sex, age group and viral suppression among persons on ART.

Results: We estimate that among 6 511 000 PLHIV in South Africa in 2012, 3 300 000 individuals (50.7%) accessed care and 32.9% received ART. Although viral suppression was 73.7% among the treated population in 2012, the overall percentage of persons with viral suppression among all PLHIV was 23.8%. Linkage to HIV care was lower among men (38.5%) than among women (57.2%). Overall, 47.1% of those aged 0-14 years and 47.0% of those aged 15-49 years were linked to care compared with 56.2% among those aged above 50 years.

Conclusion: Around a quarter of all PLHIV have achieved viral suppression in South Africa. Men and younger persons have poorer linkage to HIV care. Expanding HIV testing, strengthening prompt linkage to care and further expansion of ART are needed for South Africa to reach the 90-
Focus on these areas will reduce the transmission of new HIV infections and mortality in the general population.

Abstract access

Editor’s notes: To maximise the impact of ART, people living with HIV should be diagnosed early, enrolled and initiated on antiretroviral therapy (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.

In this manuscript, the authors used a combination of national HIV prevalence estimates and routine data collected through the National Health Laboratory Service to construct and characterize the different stages of the HIV care continuum in South Africa.

They estimate that, despite the expansion of the ART programme in South Africa, only about a quarter of people living with HIV were virally suppressed in 2012, contrasting with recent estimates from Botswana where about 70% of people living with HIV were reported to be virally suppressed. They estimate that only about half of all people living with HIV accessed care, but report that, once in care, the ART programme proves to be effective with three-quarters of people on ART achieving virologic suppression. Not surprisingly they found that men and younger persons have poorer linkage to care. They recommend that HIV testing needs to be expanded, and linkage to care needs to be promoted for people testing HIV-positive, if the UNAIDS 90-90-90 treatment target is to be reached.

This paper illustrates how, in the context of a national public sector laboratory diagnostic service, routine laboratory data can be used to monitor the public health response to HIV at a national level.

From HIV infection to therapeutic response: a population-based longitudinal HIV cascade-of-care study in KwaZulu-Natal, South Africa.


Background: Standard approaches to estimation of losses in the HIV cascade of care are typically cross-sectional and do not include the population stages before linkage to clinical care. We used individual-level longitudinal cascade data, transition by transition, including population stages, both to identify the health-system losses in the cascade and to show the differences in inference between standard methods and the longitudinal approach.

Methods: We used non-parametric survival analysis to estimate a longitudinal HIV care cascade for a large population of people with HIV residing in rural KwaZulu-Natal, South Africa. We linked data from a longitudinal population health surveillance (which is maintained by the Africa Health Research Institute) with patient records from the local public-sector HIV treatment programme (contained in an electronic clinical HIV treatment and care database, ARTemis). We followed up all people who had been newly detected as having HIV between Jan 1, 2006, and Dec 31, 2011, across six cascade stages: three population stages (first positive HIV test, HIV status knowledge, and linkage to care) and three clinical stages (eligibility for antiretroviral therapy [ART], initiation of ART, and therapeutic response). We compared our estimates to cross-sectional cascades in the same population. We estimated the cumulative incidence of reaching a particular cascade stage at a specific time with Kaplan-Meier survival analysis.
Findings: Our population consisted of 5205 individuals with HIV who were followed up for 24,031 person-years. We recorded 598 deaths. 4539 individuals gained knowledge of their positive HIV status, 2818 were linked to care, 2151 became eligible for ART, 1839 began ART, and 1456 had successful responses to therapy. We used Kaplan-Meier survival analysis to adjust for censorship due to the end of data collection, and found that 8 years after testing positive in the population, 16% had died. Among living patients, 82% knew their HIV status, 45% were linked to care, 39% were eligible for ART, 35% initiated ART, and 33% had reached therapeutic response. Median times to transition for these cascade stages were 52 months, 52 months, 20 months, 3 months, and 9 months, respectively. Compared with the population stages in the cascade, the transitions across the clinical stages were fast. Over calendar time, rates of linkage to care have decreased and patients presenting for the first time for care were, on average, healthier.

Interpretation: HIV programmes should focus on linkage to care as the most important bottleneck in the cascade. Cascade estimation should be longitudinal rather than cross-sectional and start with the population stages preceding clinical care.

Abstract access

Editor’s notes: The HIV treatment cascade outlines the stages required to effectively treat HIV, starting with HIV testing and ending with viral suppression. The cascade has become a widely-used framework to evaluate the performance of HIV care programmes, to measure progress towards universal treatment coverage, and to identify gaps in care. However, methods for constructing the HIV treatment cascade vary considerably. The majority of cascade analyses rely on cross-sectional data obtained from different sources. The authors present the first analysis of the HIV treatment cascade that follows individuals longitudinally from the time of HIV infection across all stages of the cascade. By linking data from a demographic surveillance system with electronic clinical records, they are able to describe the cascade for a large population-based cohort of people living with HIV in rural KwaZulu-Natal, South Africa. They demonstrate that, once people became eligible for ART, the rates of ART initiation, and of viral suppression after initiation, were high. Half of individuals started ART within three months of becoming eligible, and 94% of people on therapy achieved virologic suppression. In addition, retention in care improved over time. However, a key finding is that rates of HIV diagnosis and linkage to care worsened over time, and less than 50% of people had linked to care within eight years of HIV infection, despite 82% being aware of their status. As illustrated by cascade analyses in other settings, increasing linkage to care remains a major challenge for reaching the UNAIDS 90-90-90 treatment target in sub-Saharan Africa.

In addition to highlighting linkage as the most important bottleneck in the HIV care cascade in this part of rural KwaZulu-Natal, the study illustrates some of the weaknesses in traditional cascade analyses based on cross-sectional data. The cross-sectional cascade is constructed from snapshots of different groups of people in a particular moment in time, rather than describing what happens to the same group of people over time. The authors illustrate how a cross-sectional analysis can give a misleading impression of improvement in the cascade over time, because it fails to take account of changes in the population. The longitudinal cascade, by following the same group of people, provides important insights into the true progression of the cascade over time, and identification of losses along each stage. However, the individual-level longitudinal data necessary for this type of analysis requires a large investment in data collection, and is unlikely to be feasible in most resource-limited settings.
2. Elimination of childhood infections

PMTCT service uptake among adolescents and adult women attending antenatal care in selected health facilities in Zimbabwe.


Background: Age-disaggregated analyses of prevention of mother-to-child transmission (PMTCT) program data to assess the uptake of HIV services by pregnant adolescent women are limited but are critical to understanding the unique needs of this vulnerable, high risk population.

Methods: We conducted a retrospective analysis of patient-level PMTCT data collected from 2011 to 2013 in 36 health facilities in 5 districts of Zimbabwe using an electronic database. We compared uptake proportions for PMTCT services between adolescent (< 19 years) and adult (> 19 years) women. Multivariable binomial regression analysis was used to estimate the association of the women's age group with each PMTCT service indicator.

Results: The study analysed data from 22,215 women aged 12 to 50 years (22.5% adolescents). Adolescents were more likely to present to ANC before 14 weeks gestational age compared to older women (adjusted relative risk (aRR)=1.34; 95% confidence interval (CI): 1.22-1.47) with equally low rates of completion of four ANC visits. Adolescents were less likely to present with known HIV status (aRR=0.34; 95% CI: 0.29-0.41) but equally likely to be HIV tested in ANC. HIV prevalence was 5.5% in adolescents versus 20.1% in adults. While > 84% of both HIV-positive groups received ARVs for PMTCT, 44% of eligible adolescents were initiated on ART versus 51.3% of eligible adults, though not statistically significant.

Conclusions: Pregnant adolescents must be a priority for primary HIV prevention services and expanded HIV treatment services among pregnant women to achieve an AIDS-free generation in Zimbabwe and similar high HIV burden countries.

Abstract access

Editor's notes: Young women continue to be a key population at risk of acquiring HIV, and contribute approximately one-third of all new infections in sub-Saharan Africa. Young women face multiple legal, economic and social vulnerabilities that place them not only at higher risk of acquiring HIV but may also have an impact on their ability to access antenatal care (ANC) services and programmes to prevent mother-to-child HIV transmission (PMTCT) if they get pregnant. This in turns has implications for the goal of eliminating paediatric HIV infection.

This retrospective study compared the uptake of PMTCT services between adolescents (people aged 19 years and below) and older women accessing ANC in 36 public sector services across Zimbabwe. The study was conducted between 2011 and 2013, when PMTCT guidelines recommended Option A. Option A called for life-long antiretroviral therapy (ART) for women who were ART-eligible based on immunological or clinical criteria; or, for people ineligible, zidovudine monotherapy through pregnancy followed by single dose nevirapine at the onset of labour. It is no longer formally recommended by World Health Organization (WHO), although it is still used in some countries.

Nearly a quarter of all women were adolescents and over 80% were on their first pregnancy or primigravid. Adolescent women were 34% more likely to attend their first ANC visit by 14 weeks of gestational age compared to adult women. But among both groups, only about 10% attended their
first ANC visit in the first trimester and less than 40% attended the four antenatal visits recommended by WHO. Notably, knowledge of HIV status prior to the first ANC attendance was 66% lower in adolescent women, even after adjusting for parity and facility type, with only 3.1% aware of their HIV status. In addition, the proportion of women who were known HIV-positive and taking ART was also lower, although this may be due partly to fewer adolescents being eligible for ART. The uptake of HIV testing (over 95%) and uptake of zidovudine prophylaxis was high among all women. However, there was a suggestion that adolescents were less likely than older women to start ART if they were eligible, although this was not statistically significant. Indeed, several studies in the region have demonstrated lower levels of ART initiation among pregnant adolescents compared to older women.

Older women would have been more likely to have undergone HIV testing in previous pregnancies. However, even after adjusting for parity, this study demonstrates that adolescents are less likely to have previously accessed HIV testing. Common barriers to testing highlighted by other studies include lack of information, unavailability of HIV testing services, unfriendly HIV testing environments in health facilities and the need for parental consent. Lack of knowledge of HIV status prior to pregnancy is also a missed opportunity for family planning, and initiation of ART prior to pregnancy. The substantial difference in HIV prevalence among adolescents compared to older women highlights the critical need for implementing prevention programmes such as pre-exposure prophylaxis among young women in high HIV prevalence settings. While adolescents are less likely to be tested for HIV in the general population than adults, this study illustrates that when HIV testing is offered in appropriate, supportive environments, uptake is high.

Overall, the uptake of HIV testing and of prophylaxis were high, demonstrating the potential for eliminating infections in children. A major limitation is that this analysis was limited to women who had sought antenatal care. Promoting early ANC attendance is important to allow early ART initiation, to reduce the risk of intrauterine HIV transmission. Following a positive HIV test result, particular attention is necessary to ensure linkage to care and support for sustained adherence to ART.

3. Combination prevention

Discourses of masculinity, femininity and sexuality in Uganda’s Stand Proud, Get Circumcised campaign.


This paper analyses discourses of masculinity, femininity and sexuality in Stand Proud, Get Circumcised, a public health campaign promoting circumcision as an HIV-prevention strategy in Uganda. The campaign includes posters highlighting the positive reactions of women to circumcised men, and is intended to support the national rollout of voluntary medical male circumcision. We offer a critical discourse analysis of representations of masculinity, femininity and sexuality in relation to HIV prevention. The campaign materials have a playful feel and, in contrast to ABC (Abstain, Be faithful, Use condoms) campaigns, acknowledge the potential for pre-marital and extra-marital sex. However, these posters exploit male anxieties about appearance and performance, drawing on hegemonic masculinity to promote circumcision as an idealised body aesthetic. Positioning women as the campaign’s face reasserts a message that women are the custodians of family health and simultaneously perpetuates a norm of estrangement between men and their health. The wives’ slogan, ‘we have less chance of getting HIV’, is misleading, because circumcision only directly prevents female-to-male HIV transmission. Reaffirming hegemonic notions of appearance- and performance-based heterosexual masculinity reproduces existing unsafe
norms about masculinity, femininity and sexuality. In selling male circumcision, the posters fail to promote an overall HIV-prevention message.

Abstract access

Editor’s notes: In this article, the authors provide a feminist, critical discourse analysis of Uganda’s 2012 ‘Stand Proud, Get Circumcised’ campaign. The campaign promoted voluntary medical male circumcision as an HIV prevention strategy. The authors look at how masculinity, femininity, gender relations and acceptable sexuality are configured.

The authors note that even within this prevention strategy that is male-only, men were largely absent with women representing the campaign’s public face. They argue that this is in keeping with widespread messages about gender and HIV in the region that position women as the central actors. That said, messages about normative masculinity were evident and focussed on anxieties about men’s penises as a site for the physical assessment of masculine sexual prowess or failure. Together with a lack of reference to gay men, this positioning affirms dominant ideals of what a ‘man’ is: straight, circumcised, sexually active. The authors also observe that discourses of femininity, while departing from women-as-victims and introducing sexual pleasure, were relevant only for women’s ability to impose conditions for sex, thereby influencing men to circumcise. The authors therefore argue that the discourses around gender and sexuality, rather than being socially transformative, were instead positioned to produce existing norms around sex. This positioning offers little hope for creating structural changes to gender relations that might hinder HIV transmission. The authors also express concern that the posters sell circumcision, but neglect to highlight the evidence that women are not directly protected, or that other tools of prevention including condoms remain important.

Changes in male circumcision prevalence and risk compensation in the Kisumu, Kenya population, 2008-2013.


Background: Three randomized controlled trials showed that voluntary medical male circumcision (VMMC) reduces the risk of female-to-male HIV transmission by approximately 60%. However, data from communities where VMMC programs have been implemented are needed to assess changes in circumcision prevalence and whether men and women compensate for perceived reductions in risk by increasing their HIV risk behaviors.

Methods: Scale-up of free VMMC began in Kisumu, Kenya in 2008. Between 2009 and 2013, a sequence of 3 unlinked cross-sectional surveys were conducted. All individuals 15-49 years of age residing in randomly selected households were interviewed and offered HIV testing. Male circumcision status was confirmed by examination. Design-adjusted bivariate comparisons and multivariable analyses were used for statistical inference.

Results: The prevalence of male circumcision increased from 32% (95% CI: 26% to 38%) in 2009 to 60% (95% CI: 56% to 63%) in 2013. The adjusted prevalence ratio of HIV and genital ulcer disease in circumcised compared with uncircumcised men was 0.48 (95% CI: 0.36 to 0.66) and 0.51 (95% CI: 0.37 to 0.69), respectively. There was no association between circumcision status and sexual behaviors, HIV knowledge, or indicators of risk perception.

Conclusions: The conditions necessary for the VMMC program to have a significant public health impact are present in Kisumu, Kenya. Between 2009 and 2013, circumcision prevalence
increased from 30% to 60%; HIV prevalence in circumcised men was half that of uncircumcised men, and there was no or minimal sexual risk compensation.

Abstract access

Editor’s notes: Evidence of the protective effect of male circumcision on HIV incidence has led many countries in sub-Saharan Africa to promote voluntary medical male circumcision (VMMC). Mathematical models have illustrated that VMMC programmes will reduce HIV prevalence over time when VMMC uptake is high, and when men who have had VMMC do not substantially increase their sexual risk behaviours. In Kenya, the VMMC programme has exceeded its targets, with over 1.1 million procedures conducted between 2008 and 2015. In this paper, the authors assessed the assumptions behind the models, using data from three population-based cross-sectional surveys conducted among male and female adult residents of Kisumu, Kenya between 2009 and 2013. During this time, VMMC prevalence among men almost doubled from 32% to 60%, yet, HIV prevalence did not change for men or women. In addition, men who had VMMC reported the same levels of sexual risk behaviours as men who were not circumcised, yet had half the prevalence of HIV and genital ulcer disease. This study re-confirms the individual benefit of VMMC in a non-trial population, while demonstrating no evidence for sexual risk compensation. This study is notable for its large sample size, population-based sampling design, visual confirmation of circumcision status, and HIV testing protocol. Studies of longer duration are required to confirm the population-level impacts of VMMC – i.e. a protection benefit beyond men who had VMMC - on HIV prevalence, and to monitor the longer-term trend in sexual risk behaviours.

Educating religious leaders to promote uptake of male circumcision in Tanzania: a cluster randomised trial.


Background: Male circumcision is being widely deployed as an HIV prevention strategy in countries with high HIV incidence, but its uptake in sub-Saharan Africa has been below targets. We did a study to establish whether educating religious leaders about male circumcision would increase uptake in their village.

Methods: In this cluster randomised trial in northwest Tanzania, eligible villages were paired by proximity (<60 km) and the time that a free male circumcision outreach campaign from the Tanzanian Ministry of Health became available in their village. All villages received the standard male circumcision outreach activities provided by the Ministry of Health. Within the village pairs, villages were randomly assigned by coin toss to receive either additional education for Christian church leaders on scientific, religious, and cultural aspects of male circumcision (intervention group), or standard outreach only (control group). Church leaders or their congregations were not masked to random assignment. The educational intervention consisted of a 1-day seminar co-taught by a Tanzanian pastor and a Tanzanian clinician who worked with the Ministry of Health, and meetings with the study team every 2 weeks thereafter, for the duration of the circumcision campaign. The primary outcome was the proportion of male individuals in a village who were circumcised during the campaign, using an intention-to-treat analysis that included all men in the village. This trial is registered with ClinicalTrials.gov, number NCT 02167776.

Findings: Between June 15, 2014, and Dec 10, 2015, we provided education for church leaders in eight intervention villages and compared the outcomes with those in eight control villages. In the
intervention villages, 52.8% (30 889 of 58 536) of men were circumcised compared with 29.5% (25 484 of 86 492) of men in the eight control villages (odds ratio 3.2 [95% CI, 1.4-7.3]; p=0.006).

Interpretation: Education of religious leaders had a substantial effect on uptake of male circumcision, and should be considered as part of male circumcision programmes in other sub-Saharan African countries. This study was conducted in one region in Tanzania; however, we believe that our intervention is generalisable. We equipped church leaders with knowledge and tools, and ultimately each leader established the most culturally-appropriate way to promote male circumcision. Therefore, we think that the process of working through religious leaders can serve as an innovative model to promote healthy behaviour, leading to HIV prevention and other clinically relevant outcomes, in a variety of settings.

Abstract Full-text [free] access

Editor’s notes: Voluntary medical male circumcision is recommended for HIV prevention in settings with high prevalence of HIV. However, uptake of male circumcision has been lower in some settings than is optimal to reduce population-level HIV incidence. Religious beliefs can be an important barrier to acceptance of VMMC. In this community randomised trial, the investigators sought to improve uptake of male circumcision in Tanzania through an education programme delivered to religious leaders alongside a VMMC outreach campaign. Following educational seminars, each religious leader was asked to decide how best to address issues of male circumcision in his or her own community. Overall, there was a three-fold increase in uptake of male circumcision in the programme villages compared with control villages.

Deep commitment to religious faith and practices is common in many sub-Saharan countries. In this study, investigators used an innovative approach to promote healthy behaviour by tapping into the power of religious leaders. The impressive results illustrate the importance of addressing social and structural determinants of behaviour. This is a model that could be extended to address other challenging health behaviours in this and other similar settings.

4. Key populations

Factors associated with the uptake of and adherence to HIV pre-exposure prophylaxis in people who have injected drugs: an observational, open-label extension of the Bangkok Tenofovir Study.


Background: Results of the randomised, double-blind, placebo-controlled Bangkok Tenofovir Study (BTS) showed that taking tenofovir daily as pre-exposure prophylaxis (PrEP) can reduce the risk of HIV infection by 49% in people who inject drugs. In an extension to the trial, participants were offered 1 year of open-label tenofovir. We aimed to examine the demographic characteristics, drug use, and risk behaviours associated with participants' uptake of and adherence to PrEP.

Methods: In this observational, open-label extension of the BTS (NCT00119106), non-pregnant, non-breastfeeding, HIV-negative BTS participants, all of whom were current or previous injecting drug users at the time of enrolment in the BTS, were offered daily oral tenofovir (300 mg) for 1 year at 17 Bangkok Metropolitan Administration drug-treatment clinics. Participant demographics,
Drug use, and risk behaviours were assessed at baseline and every 3 months using an audio computer-assisted self-interview. HIV testing was done monthly and serum creatinine was assessed every 3 months. We used logistic regression to examine factors associated with the decision to take daily tenofovir as PrEP, the decision to return for at least one PrEP follow-up visit, and greater than 90% adherence to PrEP.

Findings: Between Aug 1, 2013, and Aug 31, 2014, 1348 (58%) of the 2306 surviving BTS participants returned to the clinics, 33 of whom were excluded because they had HIV (n=27) or grade 2-4 creatinine results (n=6). 798 (61%) of the 1315 eligible participants chose to start open-label PrEP and were followed up for a median of 335 days (IQR 0-364). 339 (42%) participants completed 12 months of follow-up; 220 (28%) did not return for any follow-up visits.

Participants who were 30 years or older (odds ratio [OR] 1.8, 95% CI 1.4-2.2; p<0.0001), injected heroin (OR 1.5, 1.1-2.1; p=0.007), or had been in prison (OR 1.7, 1.3-2.1; p<0.0001) during the randomised trial were more likely to choose PrEP than were those without these characteristics. Participants who reported injecting heroin or being in prison during the 3 months before open-label enrolment were more likely to return for at least one open-label follow-up visit than those who did not report injecting heroin (OR 3.0, 95% CI 1.3-7.3; p=0.01) or being in prison (OR 2.3, 1.4-3.7; p=0.0007). Participants who injected midazolam or were in prison during open-label follow-up were more likely to be greater than 90% adherent than those who did not inject midazolam (OR 2.2, 95% CI 1.2-4.3; p=0.02) or were not in prison (OR 4.7, 3.1-7.2; p<0.0001).

One participant tested positive for HIV, yielding an HIV incidence of 2.1 (95% CI 0.05-11.7) per 1000 person-years. No serious adverse events related to tenofovir use were reported.

Interpretation: More than 60% of returning, eligible BTS participants started PrEP, which indicates that a substantial proportion of PWID who are knowledgeable about PrEP might be interested in taking it. Participants who had injected heroin or been in prison were more likely to choose to take PrEP, suggesting that participants based their decision to take PrEP, at least in part, on their perceived risk of incident HIV infection.

Abstract access

Editor’s notes: Following the clinical trials assessing the efficacy of oral pre-exposure prophylaxis (PrEP) for HIV prevention, several of the trial teams and others have undertaken open-label extension and implementation studies. These were conducted to investigate the ‘real-world’ delivery of PrEP among key populations in various settings throughout the world. This paper presents the open-label study following the Bangkok Tenofovir Study (BTS) where oral PrEP was offered to participants, people who inject (or injected) drugs, for one year in the BTS study clinics. Unique to this study was the element of observed daily dosing at the clinics where participants were required to attend in order to access their PrEP. Results of the study are largely in line with reports from other similar studies, where people with more HIV-associated risk factors tended to adhere better and were more likely to take up and use PrEP. Interestingly, having a casual partner was not associated with better adherence, however, the number of casual partners reported by participants decreased during the study period, and there was no observed increase in other risky behaviours such as injecting drug use or sharing needles. One other additional point of note was the relatively higher adherence seen among prisoners and other incarcerated people which could point to consistent and easy access as a strong motivator to take PrEP. These results are an important contribution to the growing body of evidence around PrEP implementation which seems to suggest that people with a higher risk will be appropriately self-selecting for uptake of the programme.
HIV self-testing in Peru: questionable availability, high acceptability but potential low linkage to care among men who have sex with men and transgender women.


HIV status awareness is key to prevention, linkage-to-care and treatment. Our study evaluated the accessibility and potential willingness of HIV self-testing among men who have sex with men (MSM) and transgender women in Peru. We surveyed four pharmacy chains in Peru to ascertain the commercial availability of the oral HIV self-test. The pharmacies surveyed confirmed that HIV self-test kits were available; however, those available were not intended for individual use, but for clinician use. We interviewed 147 MSM and 45 transgender women; nearly all (82%) reported willingness to perform the oral HIV self-test. However, only 55% of participants would definitely seek a confirmatory test in a clinic after an HIV-positive test result. Further, price may be a barrier, as HIV self-test kits were available for 18 USD, and MSM and transgender women were only willing to pay an average of 5 USD. HIV self-testing may facilitate increased access to HIV testing among some MSM/transgender women in Peru. However, price may prevent use, and poor uptake of confirmatory testing may limit linkage to HIV treatment and care.

Abstract access

Editor’s notes: One of the key ways to reduce stigma around HIV is to increase uptake of HIV testing, making it more acceptable and widely available. The authors of this paper sought to understand the barriers to the use of oral self-testing HIV kits. Evidence illustrates that awareness of HIV status leads to safer sexual and injecting risk behaviours and reduced HIV prevalence. Gay men and other men who have sex with men and transgender women are often marginalized populations. They can experience increased prevalence of HIV and have poorer access to HIV testing and treatment. This descriptive study provides important information illustrating that the use of oral self-testing HIV kits are acceptable to gay men and other men who have sex with men and transgender women. On average, respondents said they would undergo testing four times a year. While test kits were available at pharmacies, the higher price prohibits frequent use. Following diagnosis with a self-test, two thirds of transgender women and 71% of gay men and other men who have sex with men said they would follow up with a confirmatory test. Strategies are necessary to encourage everyone to access services to receive confirmatory testing, counselling and referral to treatment and care as necessary. Prices of HIV self-testing kits need to be lowered to increase accessibility.

Effectiveness of peer-led interventions to increase HIV testing among men who have sex with men: a systematic review and meta-analysis.


HIV testing constitutes a key step along the continuum of HIV care. Men who have sex with men (MSM) have low HIV testing rates and delayed diagnosis, especially in low-resource settings. Peer-led interventions offer a strategy to increase testing rates in this population. This systematic review and meta-analysis summarizes evidence on the effectiveness of peer-led interventions to increase the uptake of HIV testing among MSM. Using a systematic review protocol that was developed a priori, we searched PubMed, PsycINFO and CINAHL for articles reporting original results of randomized or non-randomized controlled trials (RCTs), quasi-experimental interventions, and pre- and post-intervention studies. Studies were eligible if they
targeted MSM and utilized peers to increase HIV testing. We included studies published in or after 1996 to focus on HIV testing during the era of combination antiretroviral therapy. **Seven studies** encompassing a total of 6205 participants met eligibility criteria, including two quasi-experimental studies, four non-randomized pre- and post-intervention studies, and one cluster randomized trial. Four studies were from high-income countries, two were from Asia and only one from sub-Saharan Africa. We assigned four studies a "moderate" methodological rigor rating and three a "strong" rating. **Meta-analysis of the seven studies found HIV testing rates were statistically significantly higher in the peer-led intervention groups versus control groups (pooled OR 2.00, 95% CI 1.74-2.31).** Among randomized trials, HIV testing rates were significantly higher in the peer-led intervention versus control groups (pooled OR: 2.48, 95% CI 1.99-3.08). Among the non-randomized pre- and post-intervention studies, the overall pooled OR for intervention versus control groups was 1.71 (95% CI 1.42-2.06), with substantial heterogeneity among studies ($I^2 = 70\%$, $p < 0.02$). **Overall, peer-led interventions increased HIV testing among MSM but more data from high-quality studies are needed to evaluate effects of peer-led interventions on HIV testing among MSM in low- and middle-income countries.**

Abstract access

**Editor's notes:** One of the key challenges for the HIV response is the low uptake of HIV testing in many settings. This leads to a high proportion of individuals living with HIV being unaware of their status, failing to engage with care and treatment and hence being at risk of transmitting HIV to others. Recent reviews have illustrated that programmes led by members of the same peer group can be effective in promoting HIV-associated behavioural change and improving clinical outcomes. Gay men and other men who have sex with men can experience specific challenges associated with engagement with HIV care. This problem is particularly acute in resource poor regions due to very high levels of stigma.

This systematic review is the first to look specifically at the effectiveness of peer-led activities among gay men and other men who have sex with men. Seven studies were found which fulfilled the inclusion criteria of assessing the impact of peer-led activities on HIV testing uptake among gay men and other men who have sex with men. Four of these were in high income settings, and the others in Peru, Taiwan and Kenya. Each study illustrated a positive effect of peer-led activities on increasing HIV testing rates, and meta-analyses illustrated consistent effects when data were stratified by sub-groups (study methodology, study quality or setting). However, the generalizability of these studies to the entire population of gay men and other men who have sex with men is a concern recognized by the authors as the majority used gay-centric community venues to recruit participants. This is likely to exclude individuals who do not self-identify as being part of this community. Two studies, one in Taiwan and the other in Peru, used social-media as a mechanism of recruitment. This approach may lead to a wider recruitment, although not accessible to people without access to the internet.

Overall, this review emphasizes the potential of peer-led activities to overcome barriers to engage with testing and treatment experienced by gay men and other men who have sex with men and other hard to reach and high-risk sub-populations. It also illustrated the very limited current evidence available to assess such programmes.

**Unveiling of HIV dynamics among transgender women: a respondent-driven sampling study in Rio de Janeiro, Brazil.**

Background: The burden of HIV in transgender women (transwomen) in Brazil remains unknown. We aimed to estimate HIV prevalence among transwomen in Rio de Janeiro and to identify predictors of newly diagnosed HIV infections.

Methods: We recruited transwomen from Rio de Janeiro, Brazil, by respondent-driven sampling. Eligibility criteria were self-identification as transwomen, being 18 years of age or older, living in Rio de Janeiro or its metropolitan area, and having a valid peer recruitment coupon. We recruited 12 seed participants from social movements and formative focus groups who then used peer recruitment coupons to refer subsequent peers to the study. We categorised participants as HIV negative, known HIV infected, or newly diagnosed as HIV infected. We diagnosed syphilis in 28.9% (18.0-39.8) of participants, rectal chlamydia in 14.6% (5.4-23.8), and gonorrhoea in 13.5% (3.2-23.8). Newly diagnosed HIV infections were associated with black race (odds ratio 22.8 [95% CI 2.9-178.9]; p=0.003), travesti (34.1 [5.8-200.2]; p=0.0001) or transsexual woman (41.3 [6.3-271.2]; p=0.0001) gender identity, history of sex work (30.7 [3.5-267.3]; p=0.002), and history of sniffing cocaine (4.4 [1.4-14.1]; p=0.01).

Interpretation: Our results suggest that transwomen bear the largest burden of HIV among any population at risk in Brazil. The high proportion of HIV diagnosis among young participants points to the need for tailored long-term health-care and prevention services to curb the HIV epidemic and improve the quality of life of transwomen in Brazil.

Abstract access

Editor’s notes: This is a must-read paper for anyone interested in good participatory practices (GPP) in research and/or gender identity and HIV risk, and/or respondent driven sampling (RDS) research techniques. The researchers engaged the transwomen community from the outset in the very apt naming of the project – Transcender – and the study design – appropriate language and participant-sensitive procedures. Three community members were part of the study implementation team and the analyses were refined and written with trans community input. Although eligibility criteria included self-identification as transwomen, study participants included 131 travesti (transvestites), 107 transsexual women, 96 women, and 11 people with other gender identities. Transwomen who self-identified as women had the lowest odds of newly diagnosed HIV infection. This underscores the importance of exploring whether and how greater internal or external gender identity acceptance might confer a protective effect for HIV acquisition, perhaps through ability to use medical services through to transition, which might reduce the risk of violence. The RDS-weighted characteristics of the study participants are striking: 97% had ever experienced discrimination, 49% had ever been subjected to physical violence, and 42% had ever been raped. As for the RDS methodology itself, recruitment began with 12 seeds generating 3.6 (range two to seven) recruitment waves over a period of 26 weeks, with one seed generating 23% of the study sample. Although confidence intervals are wide, detected associations are of high magnitude and significant. With respect to homophily (the tendency to recruit others like oneself), it was moderate for HIV status and race and strong for history of sex
work. Further, what are the immediate implications of the findings? Among the 29% of participants who were newly diagnosed as having HIV, nearly half reported no previous HIV testing and 44% reported a negative HIV test in the previous year. Offering pre-exposure prophylaxis (PrEP) to the latter transwomen could have prevented them from acquiring HIV. In addition to addressing the social exclusion and marginalization that creates the structural context of HIV risk for transwomen, it is critical to achieving the UNAIDS 90-90-90 treatment target that we move effectively to remove barriers to health care access. These include fighting stigma and discrimination, tackling transphobia, penalizing and preventing physical and sexual violence, and offering immediate antiretroviral therapy to people living with HIV and to offer immediate PrEP to people found to be HIV-negative.

5. Elimination of gender inequalities

Exploring couples' processes of change in the context of SASA!, a violence against women and HIV prevention intervention in Uganda.


There is now a growing body of research indicating that prevention interventions can reduce intimate partner violence (IPV); much less is known, however, about how couples exposed to these interventions experience the change process, particularly in low-income countries. Understanding the dynamic process that brings about the cessation of IPV is essential for understanding how interventions work (or don’t) to reduce IPV. This study aimed to provide a better understanding of how couples’ involvement with SASA!−a violence against women and HIV-related community mobilisation intervention developed by Raising Voices in Uganda−influenced processes of change in relationships. Qualitative data were collected from each partner in separate in-depth interviews following the intervention. Dyadic analysis was conducted using framework analysis methods.

Study findings suggest that engagement with SASA! contributed to varied experiences and degrees of change at the individual and relationship levels. Reflection around healthy relationships and communication skills learned through SASA! activities or community activists led to more positive interaction among many couples, which reduced conflict and IPV. This nurtured a growing trust and respect between many partners, facilitating change in longstanding conflicts and generating greater intimacy and love as well as increased partnership among couples to manage economic challenges. This study draws attention to the value of researching and working with both women, men and couples to prevent IPV and suggests IPV prevention interventions may benefit from the inclusion of relationship skills building and support within the context of community mobilisation interventions.

Abstract Full-text [free] access

Editor’s notes: Evidence from sub-Saharan Africa suggests community mobilization approaches work at many different levels to prevent intimate partner violence. However it is unclear how they work. This study interviewed five couples (men and women interviewed separately) who participated in the SASA! activities and reported reductions in intimate partner violence over time. Findings suggest that engagement with SASA! by one or both members of the couple resulted in a range of change processes at the individual and relational levels. The biggest changes were seen in couples with severe intimate partner violence and in couples where one or both partners experienced high-intensity exposure to SASA! Changes were not usually universal or rapid but often uneven and slow.
Overall, greater awareness of healthy relationship values and increased relational resources – communication and self-regulation skills – led to improved relationships.

Of interest to people involved in programmes on intimate partner violence, is that focusing on promoting positive relationship values and dynamics - such as love, respect and trust are effective. Indeed, they were far more effective, than focusing on gender roles such as sharing of household tasks – which created conflict. The findings suggest intimate partner violence programmes should consider mixed-sex approaches that work with both men and women. These programmes should include promoting love and intimacy as a mechanism to achieve more balanced power in relationships and reduce violence.

Physical and sexual violence affecting female sex workers in Abidjan, Cote d'Ivoire: Prevalence, and the relationship between violence, the work environment, HIV and access to health services.


Background: Violence is a human rights violation, and an important measure in understanding HIV among female sex workers (FSW). However, limited data exist regarding correlates of violence among FSW in Cote d'Ivoire. Characterizing prevalence and determinants of violence and the relationship with structural risks for HIV can inform development and implementation of comprehensive HIV prevention and treatment programs.

Methods: FSW > 18 years were recruited through respondent driven sampling (RDS) in Abidjan, Cote d'Ivoire. In total, 466 participants completed a socio-behavioral questionnaire and HIV testing. Prevalence estimates of violence were calculated using crude and RDS adjusted estimates. Relationships between structural risk factors and violence were analyzed using chi squared tests, and multivariable logistic regression.

Results: RDS Police refusal of protection was associated with physical (adjusted Odds Ratio [aOR]:2.6; 95%CI: 1.7,4.4) and sexual violence (aOR: 3.0; 95%CI: 1.9,4.8). Blackmail was associated with physical (aOR: 2.5; 95%CI: 1.5,4.2) and sexual violence (aOR: 2.4; 95%CI: 1.5,4.0). Physical violence was associated with fear (aOR: 2.2; 95%CI: 1.3,3.1) and avoidance of seeking health services (aOR:1.7; 95%CI:1.1-2.6).

Conclusions: Violence is prevalent among FSW in Abidjan and associated with features of the work environment. These relationships highlight layers of rights violations affecting FSW, underscoring the need for structural interventions and policy reforms to improve work environments; and to address police harassment, stigma, and rights violations to reduce violence and improve access to HIV interventions.

Abstract access

Editor's notes: The authors report the findings of a study with female sex workers in Cote d'Ivoire. They explored prevalence and determinants of violence and the relationship with structural risks for HIV. Of the women interviewed, 60% had experienced physical violence and, for these women, 85% had experienced physical violence in the last 12 months. Of these women around 70% reported violence after starting sex work. Almost half of the women surveyed had experienced sexual violence. The main perpetrators were clients. There were associations between being HIV positive and physical
violence. Around 11% of the women were HIV positive but a quarter feared seeking health services due to their engagement in sex work.

A quarter of the women reported that police had refused them protection. Around a third had been intimidated or harassed by the police, and there were associations between experiences of physical or sexual violence and arrest, blackmail or condom refusal. The authors conclude that these findings illustrate an urgent need for improving the work environments for female sex workers in Cote d’Ivoire. There is also a need to address police harassment and violence. The authors argue for the need for policy reforms to address legal barriers focussing on sex work.

6. Financing

Kazakhstan can achieve ambitious HIV targets despite expected donor withdrawal by combining improved ART procurement mechanisms with allocative and implementation efficiencies.


Background: Despite a non-decreasing HIV epidemic, international donors are soon expected to withdraw funding from Kazakhstan. Here we analyze how allocative, implementation, and technical efficiencies could strengthen the national HIV response under assumptions of future budget levels.

Methodology: We used the Optima model to project future scenarios of the HIV epidemic in Kazakhstan that varied in future antiretroviral treatment unit costs and management expenditure—two areas identified for potential cost-reductions. We determined optimal allocations across HIV programs to satisfy either national targets or ambitious targets. For each scenario, we considered two cases of future HIV financing: the 2014 national budget maintained into the future and the 2014 budget without current international investment.

Findings: Kazakhstan can achieve its national HIV targets with the current budget by (1) optimally re-allocating resources across programs and (2) either securing a 35% [30%-39%] reduction in antiretroviral treatment drug costs or reducing management costs by 44% [36%-58%] of 2014 levels. Alternatively, a combination of antiretroviral treatment and management cost-reductions could be sufficient. Furthermore, Kazakhstan can achieve ambitious targets of halving new infections and AIDS-related deaths by 2020 compared to 2014 levels by attaining a 67% reduction in antiretroviral treatment costs, a 19% [14%-27%] reduction in management costs, and allocating resources optimally.

Significance: With Kazakhstan facing impending donor withdrawal, it is important for the HIV response to achieve more with available resources. This analysis can help to guide HIV response planners in directing available funding to achieve the greatest yield from investments. The key changes recommended were considered realistic by Kazakhstan country representatives.

Abstract Full-text [free] access

Editor’s notes: The HIV epidemic in Kazakhstan is concentrated around key populations (such as people who inject drugs, female sex workers and their partners, gay men and other men who have sex with men). Unlike in other settings, incidence has not decreased in recent years. However, as
Kazakhstan continues to boom economically, international donors are expected to withdraw from the country in the near future and the responsibility for funding HIV-associated programmes will shift towards the state. This article attempts to explore how different kinds of efficiencies in the distribution of resources could strengthen the national HIV response in the coming years.

The authors modelled future scenarios of the epidemic in Kazakhstan. They looked at whether and how the country could achieve certain targets by 2020 given its budgetary restrictions. They found that the country could achieve its national targets by either securing a 35% reduction in antiretroviral therapy or reducing management costs by 44%.

The topic this paper covers raises a number of important issues. As national governments move towards covering the totality of spending on HIV prevention and treatment, they will be confronted with the need to fund (using national tax revenues) prevention mechanisms. Their mechanisms are aimed at key populations who are often marginalized. Although funding these types of programmes through donor funding may have not caused political challenges, doing so using the state’s funding may. Government budget allocation is often a highly contentious exercise. Potential shifts in national priority setting following donor withdrawal should not be ignored.

As prevention programmes cover people in key populations who are easier to reach, efforts should shift towards making prevention available to the harder-to-reach sections of key populations. However, this will further increase unit costs per person reached, and probably per infection averted. Given the decrease in external funding for Kazakhstan, it is important for the national response to budget for these additional costs. This is a necessity to ensure equity in the access to the HIV response.

The costs of providing antiretroviral therapy services to HIV-infected individuals presenting with advanced HIV disease at public health centres in Dar es Salaam, Tanzania: Findings from a randomised trial evaluating different health care strategies.


Background: Understanding the costs associated with health care delivery strategies is essential for planning. There are few data on health service resources used by patients and their associated costs within antiretroviral (ART) programmes in Africa.

Material and methods: The study was nested within a large trial, which evaluated screening for cryptococcal meningitis and tuberculosis and a short initial period of home-based adherence support for patients initiating ART with advanced HIV disease in Tanzania and Zambia. The economic evaluation was done in Tanzania alone. We estimated costs of providing routine ART services from the health service provider's perspective using a micro-costing approach. Incremental costs for the different novel components of service delivery were also estimated. All costs were converted into US dollars (US$) and based on 2012 prices.

Results: Of 870 individuals enrolled in Tanzania, 434 were enrolled in the intervention arm and 436 in the standard care/control arm. Overall, the median (IQR) age and CD4 cell count at enrolment were 38 [31, 44] years and 52 [20, 89] cells/mm³, respectively. The mean per patient costs over the first three months and over a one year period of follow up following ART initiation in the standard care arm were US$ 107 (95%CI 101-112) and US$ 265 (95%CI 254-275) respectively. ART drugs, clinic visits and hospital admission constituted 50%, 19%, and 19% of the total cost per patient year, while diagnostic tests and non-ART drugs (co-trimoxazole) accounted for 10% and 2% of total per
patient year costs. The incremental costs of the intervention to the health service over the first three months was US$ 59 (p<0.001; 95%CI 52-67) and over a one year period was US$ 67(p<0.001; 95%CI 50-83). This is equivalent to an increase of 55% (95%CI 51%-59%) in the mean cost of care over the first three months, and 25% (95%CI 20%-30%) increase over one year of follow up.

Abstract  Full-text [free] access

Editor’s notes: There are very few data on the cost of providing HIV treatment in sub-Saharan Africa. The authors of this paper analysed cost data from a trial of screening services for opportunistic infections, to estimate the additional costs of HIV treatment to the health service. The most costly part of treatment was the antiretroviral medicines themselves, followed by clinic visits and hospital admissions. Diagnostic tests and treatments for other conditions were relatively inexpensive. The overall costs of treatment to the health system were fairly low in absolute terms. At around US$67 per year this is on the cheaper side of many cost studies. However, HIV treatment increases overall health system costs by a quarter. This could have significant implications for health system funding requirements in Tanzania as treatment is offered to the many people who need it in the UNAIDS 90-90-90 treatment target.

7. Health systems and services

Effect of antiretroviral therapy on malaria incidence in HIV-infected Ugandan adults.

Introduction: Using the data of a trial on cotrimoxazole (CTX) cessation, we investigated the effect of different antiretroviral therapy (ART) regimens on the incidence of clinical malaria.

Methods: During the cotrimoxazole cessation trial (ISRCTN44723643), HIV-infected Ugandan adults with CD4 at least 250 cells/µl were randomized to receive either CTX prophylaxis or placebo and were followed for a median of 2.5 years. Blood slides for malaria microscopy were examined at scheduled visits and at unscheduled visits when the participant felt unwell. CD4 cell counts were done 6-monthly. Malaria was defined as fever with a positive blood slide. ART regimens were categorized as nucleoside reverse transcriptase inhibitor (NRTI) only, non-nucleoside reverse transcriptase inhibitor (NNRTI)-containing or protease inhibitor containing. Malaria incidence was calculated using random effects Poisson regression to account for clustering of events.

Results: Malaria incidence in the three ART regimen groups was 9.9 (3.6-27.4), 9.3 (8.3-10.4), and 3.5 (1.6-7.6) per 100 person-years, respectively. Incidence on protease inhibitors was lower than that on the other regimens with the results just reaching significance (adjusted rate ratio 0.4, 95% confidence interval = 0.2-1.0, comparing with NNRTI regimens). Stratification by CTX/placebo use gave similar results, without evidence of an interaction between the effects of CTX/placebo use and ART regimen. There was no evidence of an interaction between ART regimen and CD4 cell count.

Conclusion: There was some evidence that protease inhibitor-containing ART regimens may be associated with a lower clinical malaria incidence compared with other regimens. This effect was not modified by CTX use or CD4 cell count. The antimalarial properties of protease inhibitors may have clinical and public health importance.
**Editor’s notes:** HIV protease inhibitors (PIs) have been shown to kill various life cycle stages of the malaria parasite both in vitro and in vivo at therapeutic drug levels. A randomized controlled trial in children previously illustrated that PI-based antiretroviral therapy (ART) was associated with a lower risk of recurrent malaria compared to non-nucleoside reverse transcriptase inhibitor (NNRTI)-based ART.

This study is the first to present data illustrating a reduction in clinical malaria incidence in adults on a PI-based regimen. The authors used data from the COSTOP trial, which was originally designed to look at the safety of discontinuing trimethoprim-sulfamethoxazole (TMP-SMX, Septrin) in HIV-positive Ugandan adults with a CD4 cell count ≥250 cells/µL. A limitation is that only 4% of study participants were on a PI-based ART regimen, so numbers are small. In addition, the authors were unable to adjust for potential confounders relating to individual health status. However, this analysis is a useful addition to the evidence base, suggesting that PIs may have antimalarial properties of clinical and public health importance, especially settings with high malaria transmission and moderate to high HIV prevalence.

**Stool Xpert® MTB/RIF test for the diagnosis of childhood pulmonary tuberculosis at primary clinics in Zimbabwe.**


Objective: To evaluate the diagnostic performance of Xpert®MTB/RIF on stool samples from children with clinical suspicion of pulmonary tuberculosis (PTB) at primary care clinics.

Design: A cross-sectional diagnostic evaluation enrolling 5-16 year olds from whom one induced sputum (IS) sample was tested for microbiological TB confirmation. Results of a single stool sample tested using Xpert® were compared against microbiologically confirmed TB, defined as a positive result on sputum microscopy and/or culture and/or IS Xpert®.

Results: Of 222 children enrolled, 218 had complete microbiological results. The median age was 10.6 years (interquartile range 8-13). TB was microbiologically confirmed in 19/218 (8.7%) children. Of these, respectively 5 (26%), 9 (47%) and 15 (79%) were smear-, culture- and IS Xpert®-positive. **Stool Xpert® was positive in 13/19 (68%) microbiologically confirmed cases** and 4/199 (2%) microbiologically negative cases. Stool Xpert® detected 76.9% (10/13) of human immunodeficiency virus (HIV) infected and 50% (3/6) of non-HIV-infected children with microbiologically confirmed TB (P = 0.241).

Conclusion: Stool Xpert® is a potential alternative screening test for children with suspected TB if sputum is unavailable. Strategies to optimise the diagnostic yield of stool Xpert® assay need further study.
Background: Tuberculosis (TB) continues to result in high morbidity and mortality in children from resource-limited settings. Diagnostic challenges, including resource-intense sputum collection methods and insensitive diagnostic tests, contribute to diagnostic delay and poor outcomes in children. We evaluated the diagnostic utility of stool Xpert® MTB/RIF (Xpert) compared with bacteriologic confirmation (combination of Xpert and culture of respiratory samples).

Methods: In a hospital-based study in Cape Town, South Africa, we enrolled children younger than 13 years of age with suspected pulmonary TB from April 2012- August 2015. Standard clinical investigations included tuberculin skin test, chest radiograph and HIV testing. Respiratory samples for smear microscopy, Xpert and liquid culture included gastric aspirates, induced sputum, nasopharyngeal aspirates and expectorated sputum. One stool sample per child was collected and tested using Xpert.

Results: Of 379 children enrolled (median age, 15.9 months, 13.7% HIV-infected), 73 (19.3%) had bacteriologically confirmed TB. The sensitivity and specificity of stool Xpert® vs. overall bacteriologic confirmation were 31.9% (95% CI 21.84-44.50%) and 99.7% (95% CI 98.2-100%) respectively. 23/51 (45.1%) children with bacteriologically confirmed TB with severe disease were stool Xpert® positive. Cavities on chest radiograph were associated with Xpert stool positivity regardless of age and other relevant factors (OR 7.05; 95% CI 2.16-22.98; p=0.001).

Conclusions: Stool Xpert® can rapidly confirm TB in children who present with radiologic findings suggestive of severe TB. In resource-limited settings where children frequently present with advanced disease, Xpert on stool samples could improve access to rapid diagnostic confirmation and appropriate treatment.

Abstract access

Editor’s notes: It has been known for a long time that Mycobacterium tuberculosis can be detected in stool specimens in some people with pulmonary TB disease. This is because sputum is often swallowed and M. tuberculosis bacilli can survive transit through the gastrointestinal tract. With the challenges of detecting TB in children, and the introduction of molecular diagnostic tools, there has been renewed interest in using stool specimens to improve TB diagnosis.

These two studies from southern Africa evaluated the diagnostic yield and accuracy of Xpert® MTB/RIF testing on stool specimens in children with symptoms compatible with intrathoracic TB. The study populations were different. The children in the South African study were younger than in the Zimbabwean study (median age 16 months vs. 10 years). In South Africa, only one in seven children was HIV positive whereas half the children were HIV positive in the Zimbabwean study. The South African study was conducted at hospital level whereas the Zimbabwean study was at primary health care clinics.

Despite these differences, the main findings were similar. Stool Xpert® was positive in six percent in South Africa and eight percent in Zimbabwe. Sensitivity of stool Xpert® compared to a single culture from induced sputum was 50% in South Africa and 67% in Zimbabwe. A single Xpert® test on stool was no better than a single Xpert® test on induced sputum. There was some evidence from both studies that sensitivity was higher in HIV positive children. However, in South Africa, sensitivity compared to any bacteriological confirmation was substantially lower (32%), as the reference standard included Xpert® and culture tests on multiple specimens. Sensitivity compared to the clinical decision to treat for TB was even lower (14%). This may have reflected the fact that all children in the South African study had chest X-rays and there were several children with intrathoracic lymph node disease.
What does this tell us about the role of Xpert® testing on stool for TB diagnosis in children? The evidence does not seem to provide strong support for scaling up stool Xpert® testing within standard diagnostic algorithms. As the South African study demonstrated, many of the children with positive Xpert® on stool were older children with more severe pulmonary disease. These are the children that may be more likely to produce sputum, and are the ones where we would want to make every effort to get respiratory specimens. This is especially the case in HIV-positive children, among whom there may be many possible diagnoses. Added to all this is the fact that processing and testing stool in the laboratory is not simple, meaning it might be difficult to scale up within decentralised laboratory systems.

It is encouraging that research groups are now addressing the challenge of TB diagnosis in children. It would seem that testing stool specimens for now does not really address the fundamental challenge in children, that they usually have paucibacillary disease often with little or no involvement of the lung parenchyma. The search must go on for better diagnostic tests for TB in children.


The correlation between mental health and sexual risk behaviours for HIV infection remains largely unknown in low and middle income settings. The present study determined the prevalence of psychological distress (PD) in a sub-Saharan African population with a generalized HIV epidemic, and investigated associations with HIV acquisition risk and uptake of HIV services using data from a cross-sectional survey of 13 252 adults. PD was measured using the Shona Symptom Questionnaire. Logistic regression was used to measure associations between PD and hypothesized covariates. The prevalence of PD was 4.5% (95% CI 3.9-5.1%) among men, and 12.9% (95% CI 12.2-13.6%) among women. PD was associated with sexual risk behaviours for HIV infection and HIV-infected individuals were more likely to suffer from PD. Amongst those initiated on anti-retroviral therapy, individuals with PD were less likely to adhere to treatment (91 vs. 96%; age- and site-type-adjusted odds ratio = 0.38; 95% CI 0.15, 0.99). Integrated HIV and mental health services may enhance HIV care and treatment outcomes in high HIV-prevalence populations in sub-Saharan Africa.

Abstract access

Editor’s notes: Psychological distress can lead to increased use of alcohol and drugs, sexual risk behaviour, and hence increased risk of HIV acquisition. In rural Manicaland, the fifth survey round of an open population cohort measured psychological distress for the first time in 2009-2011, following the Zimbabwe hyperinflation crisis of 2008-2009.

Psychological distress was highly prevalent, especially among women, as was HIV infection. Overall, HIV prevalence was 12.7% in men and 18.3% in women. Psychological distress and HIV were also clearly associated. Among people with psychological distress HIV prevalence was 18.8% for men and 27.2% for women, compared to 12.4% and 17.1% for men and women respectively without psychological distress.

People living with HIV (identified by anonymous testing) who had psychological distress were more likely to have had an HIV test than people without psychological distress, although this could be reversed to mean that people with HIV who knew their status were more likely to have psychological distress.
distress than people who did not. If diagnosed and on antiretroviral therapy, people with psychological distress also had poorer adherence, supporting findings of other studies.

A main challenge to interpreting these results is a lack of information on poverty and how it may have impacted both psychological distress and risk of HIV acquisition. Only one survey round used the Shona Symptom Questionnaire so the study is essentially a cross-sectional survey. Women with psychological distress were more likely to have transactional sex, engage in sex work and not use condoms, but it is not clear that these behaviours were consequences of psychological distress. Instead, both the behaviours and the distress could have been caused by poverty constraints and lack of options. The only economic variables measured were time of year (as a proxy for food availability) and employment status (employed/unemployed). Being employed was associated with lower risk of psychological distress for women, but had no effect for men.