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

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

Depression at antiretroviral therapy initiation and clinical outcomes among a cohort of Tanzanian women living with HIV.


Objective: The objective of the study was to assess the relationship of depression at antiretroviral therapy (ART) initiation with mortality and clinical outcomes among Tanzanian women living with HIV.

Design: We conducted a prospective cohort study of 1487 women who initiated ART in Dar es Salaam, Tanzania.

Methods: Symptoms of depression and anxiety were assessed using a Tanzanian-adapted and validated version of the Hopkins Symptom Checklist. Participants attended monthly clinic visits during the first 2 years of ART and CD4 T-cell counts were assessed every 4 months. Proportional hazard models were used to assess the relationship of depression with mortality and clinical outcomes.

Results: Symptoms consistent with depression were prevalent among 57.8% of women at ART initiation. After multivariate adjustment, including social support and stigma, depression at ART initiation was associated with increased risk of mortality [hazard ratio (HR): 1.92; 95% confidence interval (CI): 1.15-3.20; P = 0.01] and incidence of severe anemia (hemoglobin <8.5 g/dl; HR: 1.59; 95% CI: 1.07-2.37; P = 0.02). Under the assumption of causality, we estimate 36.1% (95% CI: 13.6-55.1%) of deaths among the study cohort were attributable to depression and its consequences. Depression was not significantly associated with trajectory of CD4 T-cell reconstitution or the risk of immunologic failure (P values >0.05).

Conclusion: Elimination of depression may reduce mortality during the first 2 years of ART by one-third in our study cohort. Randomized trials and rigorous implementation studies are needed to evaluate the individual and population-level effects of integrated mental health interventions and HIV treatment approaches in resource-limited settings.

Abstract access

Editor’s notes: People living with HIV are more than twice as likely to have depression than the general population, in both high- and low-income settings. Many studies in high-income countries have illustrated that depression is associated with poor HIV-associated outcomes. There have been relatively few longitudinal studies on this from low-income settings. This study, among women in Tanzania living with HIV, found that over half had symptoms consistent with depression at ART initiation, and this was associated with a two-fold risk of mortality. The results suggest that effective programmes which address depression, such as problem-solving therapy or cognitive behaviour therapy, at ART initiation, could have a considerable impact on mortality. There is a need to evaluate appropriate mental health programmes integrated with HIV strategies in resource-limited settings that address the specific needs of different populations of people living with HIV, such as children and adolescents

Mortality in children with human immunodeficiency virus initiating treatment: a six-cohort study in Latin America.
Objectives: To assess the risks of and factors associated with mortality, loss to follow-up, and changing regimens after children with HIV infected perinatally initiate combination antiretroviral therapy (cART) in Latin America and the Caribbean.

Study design: This 1997-2013 retrospective cohort study included 1174 antiretroviral therapy-naive, perinatally infected children who started cART when they were younger than 18 years of age (median 4.7 years; IQR 1.7-8.8) at 1 of 6 cohorts from Argentina, Brazil, Haiti, and Honduras, within the Caribbean, Central and South America Network for HIV Epidemiology. Median follow-up was 5.6 years (IQR 2.3-9.3). Study outcomes were all-cause mortality, loss to follow-up, and major changes/interruption/stopping of cART. We used Cox proportional hazards models stratified by site to examine the association between predictors and times to death or changing regimens.

Results: Only 52% started cART at younger than 5 years of age; 19% began a protease inhibitor. At cART initiation, median CD4 count was 472 cells/mm$^3$ (IQR 201-902); median CD4% was 16% (IQR 10-23). Probability of death was high in the first year of cART: 0.06 (95% CI 0.04-0.07). Five years after cART initiation, the cumulative mortality incidence was 0.12 (95% CI 0.10-0.14). Cumulative incidences for loss to follow-up and regimen change after 5 years were 0.16 (95% 0.14-0.18) and 0.30 (95% 0.26-0.34), respectively. Younger children had the greatest risk of mortality, whereas older children had the greatest risk of being lost to follow-up or changing regimens.

Conclusions: Innovative clinical and community approaches are needed for quality improvement in the pediatric care of HIV in the Americas.

Abstract access

Editor’s notes: Despite the dramatic declines in mortality with antiretroviral therapy (ART), mortality rates among children living with HIV still remain substantially higher than in the general paediatric population in high-income settings, such as in the United States of America. Mortality rates after ART initiation are even higher in sub-Saharan Africa, likely because children initiate ART at older ages and at more advanced stages of disease. There are, however, no data available for Latin America and the Caribbean, which has had a mostly stable epidemic with a slowly declining adult HIV incidence over the past decade.

In this retrospective cohort study, the authors investigate mortality, loss-to-follow-up (LTFU) and regimen change among children who acquired HIV in the perinatal period from Argentina, Haiti, Honduras and Brazil. They initiated ART aged below 18 years. About half of all children started ART aged over five years, and a third had clinical AIDS by the time they initiated ART. This would suggest that paediatric HIV programmes in this region face similar challenges to those seen in African programmes, including failure of prevention of mother-to-child HIV transmission (PMTCT) programmes and late diagnosis of children.

As expected, a low baseline CD4 count and clinical AIDS at baseline were both associated with an increased risk of mortality. Importantly, younger age at starting ART was also associated with an increased hazard of death, as was being an adolescent (although the association was weaker). The most likely reason for this is that the youngest children placed on ART may have been initiated following presentation with fast-progressing disease, and would therefore have a higher risk of death.
than comparatively healthier and stable older children. The higher risk of death among the adolescents likely reflects delayed diagnosis of slow-progressors in adolescence.

Another important finding was the significantly higher risk of LTFU and regimen change in adolescents compared to younger children. This finding, also noted in African and high-income setting cohorts, highlights the challenges of retaining adolescents in care, addressing treatment fatigue, and possibly increased risk of attrition from care during transitioning from paediatric to adult services.

In summary, HIV care outcomes in children in Latin America and the Caribbean appear to be similar to those reported in other settings. Together, they highlight the pressing need for strengthening prevention of mother-to-child HIV transmission programmes, particularly follow-up and prompt testing of HIV-exposed infants. It also emphasizes the need for innovative approaches to support children to stay in care and maintain long-term adherence.

High acceptability of HIV self-testing among technical vocational education and training college students in Gauteng and North West province: what are the implications for the scale up in South Africa?


Background: Although HIV self-testing (HIVST) is globally accepted as an important complement to existing HIV testing approaches, South Africa has lagged behind in its adoption. As a result, data on the acceptability and uptake of HIVST is limited. The study investigated the acceptability of HIVST among students in Technical Vocational Education and Training (TVET) colleges in two provinces in South Africa.

Methods: A cross-sectional survey using a self-administered structured questionnaire was used to collect data among 3662 students recruited from 13 TVET colleges.

Results: The mean age of the students was 21.9 years. The majority (80.9%) were sexually active; while 66.1% reported that they had one sexual partner, and 33.9% had two or more sexual partners in the past year, and 66.5% used condoms during the last sexual act. Three-quarters tested for HIV in the past year but less than half knew about HIVST prior to the survey. The acceptability of HIVST was high; about three-quarters showed a willingness to purchase a self-test kit and a majority would self-test with partners. Acceptability of HIVST was associated with being sexually active (OR = 1.73, p = 0.02, confidence interval (CI): 1.08-2.75), having ever been tested for HIV (OR = 1.74, p = 0.001, CI: 1.26-2.38), and having multiple sexual partners (OR = 0.61, p = 0.01, CI: 0.42-0.88). Three-quarters would confirm test results at a local health facility. In terms of counselling, telephone hotlines were acceptable to only 39.9%, and less than half felt that test-kit leaflets would provide sufficient information to self-test.

Interpretations: The high acceptability of HIVST among the students calls for extensive planning and preparation for the scaling up of HIVST in South Africa. In addition, campaigns similar to those conducted to promote HIV counselling and testing (HCT) should be considered to educate communities about HIVST.

Abstract Full-text [free] access

Editor's notes: The percentage of people living with HIV who know their status (the first 90 of the UNAIDS 90:90:90 treatment target) has been consistently well below the stated target in national HIV treatment cascades. HIV self-testing is an exciting strategy being used to increase the uptake of
testing, and has recently been adopted in South Africa. This study had two aims; firstly to assess the participants attitudes to currently available HIV counselling and testing services and secondly to assess the level of acceptability of HIV self-testing. The study population were students in technical and vocational education and training colleges in South Africa.

Among people who had not tested for HIV in the past year, reasons given for non-uptake of testing (other than a low perception of risk) included a fear of stigma associated with a positive test or a lack of comfort with testing in a hospital setting. Less than half of participants had heard of HIV self-testing, but when the concept was explained to them, around 80% expressed a willingness to use it if it was available, and 70% were willing to purchase the self-test kit. These results are consistent with other studies of HIV self-testing uptake and acceptability in sub-Saharan Africa.

The stated willingness of participants to present at a clinic for a confirmatory test is encouraging. However, this may not reflect actual behaviour, especially in a setting where there is currently no plan or system to link people with positive HIV self-test results to a clinic for confirmatory testing. However, the drive to improve counselling and linkage around self-testing needs to be balanced against the fundamental principle for HIV self-testing to allow choice for users to test without the need for a health worker to be present, and the privacy associated with this. Further work may include assessing acceptability of using remote services to complement HIV self-testing such as telephone hotlines or other counselling strategies.

Community mobilization for HIV testing uptake: results from a community randomized trial of a theory-based intervention in rural South Africa.


Background: HIV testing uptake in South Africa is below optimal levels. Community mobilization (CM) may increase and sustain demand for HIV testing, however, little rigorous evidence exists regarding the effect of CM interventions on HIV testing and the mechanisms of action.

Methods: We implemented a theory-driven CM intervention in 11 of 22 randomly-selected villages in rural Mpumalanga Province. Cross-sectional surveys including a community mobilization measure were conducted before (n = 1181) and after (n = 1175) a 2-year intervention (2012-2014). We assessed community-level intervention effects on reported HIV testing using multilevel logistic models. We used structural equation models to explore individual-level effects, specifically whether intervention assignment and individual intervention exposure were associated with HIV testing through community mobilization.

Results: Reported testing increased equally in both control and intervention sites: the intervention effect was null in primary analyses. However, the hypothesized pathway, CM, was associated with higher HIV testing in the intervention communities. Every standard deviation increase in village CM score was associated with increased odds of reported HIV testing in intervention village participants (odds ratio: 2.6, P = <0.001) but not control village participants (odds ratio: 1.2, P = 0.53). Structural equation models demonstrate that the intervention affected HIV testing uptake through the individual intervention exposure received and higher personal mobilization scores.

Conclusions: There was no evidence of community-wide gains in HIV testing due to the intervention. However, a significant intervention effect on HIV testing was noted in residents who were personally exposed to the intervention and who evidenced higher community
mobilization. Research is needed to understand whether CM interventions can be diffused within communities over time.

Abstract  Full-text [free] access

Editor’s notes: HIV testing is an integral component of HIV prevention strategies, and essential for achieving the UNAIDS 90-90-90 treatment target. However, testing coverage in many parts of sub-Saharan Africa remains low, particularly among men. Stigma, gender norms, and lack of ‘buy in’ about the benefits of early testing and treatment remain major barriers to testing.

This cluster-randomised trial of a community mobilization (CM) approach for HIV prevention in South Africa is one of the first to be based around an explicit theoretical model of community change. CM is designed to engage community members and motivate people to achieve a common goal, and has been used successfully in some HIV prevention programmes. The programme focused on young men aged 18-35 years, with an aim to build community support for normative changes that are necessary to tackle social barriers to HIV testing and care. Trial outcomes included gender norms, sexual behaviour and HIV testing uptake. The trial found no overall effect on the uptake of HIV testing – self-reported HIV testing increased significantly in both arms over the two year observation period, with no difference between the programme and control communities. However, CM scores, used to quantify the degree of community engagement, were higher in the programme communities. In addition, individuals with greater exposure to the programme were more likely to report HIV testing. These findings suggest that although the CM programme did have an impact on the individuals exposed to it, the effect did not filter through to the wider community.

CM strategies are used increasingly in public health programmes, and can be a powerful tool for increasing community awareness and engagement with HIV prevention. The benefit of CM is its ability to diffuse beyond the immediate participants to the community as a whole, to bring about the greatest possible change. However, little is known about why and how these approaches work. As this study illustrates, there is a need to understand more about the underlying mechanisms of change associated with CM, and the factors that contribute to its success.


Background: Few studies have examined multidrug-resistant (MDR) tuberculosis (TB) treatment outcomes among HIV-infected persons after widespread expansion of antiretroviral therapy (ART). We describe MDR-TB treatment outcomes among HIV-infected and HIV-uninfected patients in Botswana after ART expansion.

Methods: We retrospectively reviewed data from patients who started MDR-TB therapy in Botswana during 2006-2013. Multivariable regression models were used to compare treatment outcomes between HIV-infected and HIV-uninfected patients.

Results: We included 588 MDR-TB patients in the analysis, of whom, 47 (8.0%) and 9 (1.5%) were diagnosed with pre-extendibly drug-resistant (XDR)-TB and XDR-TB, respectively. Of the 408 (69.4%) HIV-infected patients, 352 (86.0%) were on ART or started ART during treatment, and median baseline CD4 T-cell count was 234 cells/mm³. Treatment success rates were 79.4% and 73.0% among HIV-uninfected and HIV-infected patients, respectively (P = 0.121). HIV-infected
patients with CD4 T-cell count <100 cells/mm\(^3\) were more likely to die during treatment compared with HIV-uninfected patients (adjusted risk ratio = 1.890; 95% CI: 1.098 to 3.254).

Conclusions: High rates of treatment success were achieved with programmatic management of MDR-TB and HIV in Botswana after widespread expansion of ART. However, a 2-fold increase in mortality was observed among HIV-infected persons with baseline CD4 <100 cells/mm\(^3\) compared with HIV-uninfected persons.

Abstract access

**Editor’s notes:** This article describes the treatment outcomes of multidrug-resistant tuberculosis (MDR-TB) among HIV-positive and HIV-negative people in Botswana between 2006 and 2013, after expansion of the antiretroviral therapy (ART) programme. The investigators used programmatic data for their analysis, and the results therefore reflect “real-life” experience of people in the MDR-TB programme.

The authors found very high rates of treatment success. Some 75% of people started on MDR-TB treatment achieved treatment success, and among people living with HIV the success rate was 73%. This is significantly higher than the 57% treatment success reported in a recent systematic review of HIV-positive MDR-TB people. Pre-treatment counselling, strict directly observed therapy, food and transport incentives, follow-up of people who missed their monthly consultations are all aspects of the MDR-TB (and ART programme) that may have contributed to these high success rates. On the other hand, the inclusion of studies done before widespread access to ART may have contributed to the lower success rates reported in the systematic review.

The reported treatment success of 79% among HIV-negative people was lower than the 84-89% treatment success reported for the new nine-month MDR-TB regimen endorsed by WHO. However, the authors emphasize that additional research is necessary to evaluate the effectiveness of the nine-month regimen in a similar setting as Botswana, where the majority of MDR-TB people are HIV-positive.

In this study, about 70% of MDR-TB people were HIV-positive, and 20% of people had a CD4 count of less than 100 cells/mm\(^3\) at the time of MDR-TB treatment initiation. People with a CD4 less than 100 cells/mm\(^3\) were almost twice as likely to die during their MDR-TB treatment compared to HIV-negative people. People living with HIV, with CD4<100 cells/mm\(^3\) often have co-morbidities, and are at high risk of dying of diseases other than TB, including cryptococcal meningitis and other opportunistic infections. The authors suggest that additional research is necessary to improve the clinical management of MDR-TB people with advanced immunosuppression.

The authors conclude that to reduce mortality from MDR-TB and other causes, increased efforts are necessary to reach all people living with HIV with ART as part of comprehensive HIV care. In June 2016, Botswana launched the “Test and Treat” programme, to provide ART to all people living with HIV, which should contribute to this goal.

**Barriers to care and 1-year mortality among newly-diagnosed HIV-infected people in Durban, South Africa.**

Background: Prompt entry into HIV care is often hindered by personal and structural barriers. Our objective was to evaluate the impact of self-perceived barriers to healthcare on 1-year mortality among newly diagnosed HIV-infected individuals in Durban, South Africa.

Methods: Prior to HIV testing at four outpatient sites, adults (≥18y) were surveyed regarding perceived barriers to care including: 1) service delivery; 2) financial; 3) personal health perception; 4) logistical; and 5) structural. We assessed deaths via phone calls and the South African National Population Register. We used multivariable Cox proportional hazards models to determine the association between number of perceived barriers and death within one year.

Results: 1899 HIV-infected participants enrolled. Median age was 33 years (IQR: 27-41y), 49% were female, and median CD4 count was 192/µl (IQR: 72-346/µl). 1057 participants (56%) reported no, 370 (20%) reported 1-3, and 460 (24%) reported >3 barriers to care. By one year, 250 (13%, 95% CI: 12%, 15%) participants died. Adjusting for age, sex, education, baseline CD4 count, distance to clinic, and TB status, participants with 1-3 barriers (adjusted hazard ratio [aHR]: 1.49, 95% CI: 1.06, 2.08) and >3 barriers (aHR: 1.81, 95% CI: 1.35, 2.43) had higher 1-year mortality risk compared to those without barriers.

Conclusions: HIV-infected individuals in South Africa who reported perceived barriers to medical care at diagnosis were more likely to die within one year. Targeted structural interventions such as extended clinic hours, travel vouchers, and streamlined clinic operations may improve linkage to care and ART initiation for these people.

Abstract access

Editor’s notes: Mortality among people living with HIV remains high in South Africa. Suboptimal engagement in HIV care is noted to be a significant contributor to this, with many deaths occurring before people have even started antiretroviral therapy. Potential barriers to care range from personal, such as perceived good health therefore believing antiretroviral therapy is not necessary, to logistical, such as a lack of transportation, to structural barriers such as busy clinics and long waits for care. Barriers perceived by the patient may also be different to barriers perceived by providers of care.

This study sought to explore self-perceived barriers to care at the time of testing for HIV and their impact on one-year mortality. This was in the context of a trial testing whether or not health system navigators improved linkage to and retention in care. Between 2010 and 2013, adults attending for HIV testing across four clinics in Durban, South Africa enrolled in this trial, completed a baseline questionnaire. This examined self-perceived barriers to care, their emotional health and social support. Participants found to be HIV positive were followed up via phone within 12 months. Limited clinical data was sought from clinic notes. Any reported deaths were confirmed by a national register.

Some 1887 participants were enrolled and subsequently diagnosed with HIV. Some 250 people died by 12 months post enrollment. A myriad of barriers were reported, the most common being associated with personal health, service delivery and structural issues. However, it was the sum of barriers that was predictive of risk. People with one or more perceived barriers had a higher one-year mortality risk compared to people without perceived barriers. Furthermore, it was illustrated that the greater the number of perceived barriers, the greater the risk of mortality. The risk for people with greater than three perceived barriers was double that of people with three or less barriers (22% versus 11%). Interestingly, there was no significant impact of emotional and social support as reported at baseline.

Limitations noted by the authors include a possible overestimation of deaths attributable to HIV, since there were no specific data on the cause of death. Data on co-morbidities (apart from tuberculosis)
were also not collected and their potential impact on mortality is not addressed. However, it may be fair to assume that any barriers to HIV care would also extend to affecting access to other forms of healthcare. Overall, the study highlights perceived barriers at diagnosis as plausible factors to address when shaping programmes to improve retention in care.

2. Combination prevention

How presentation of drug detection results changed reports of product adherence in South Africa, Uganda and Zimbabwe.


Accurate estimates of study product use are critical to understanding and addressing adherence challenges in HIV prevention trials. The VOICE trial exposed a significant gap between self-reported adherence and drug detection. The VOICE-D qualitative study was designed to better understand non-adherence during VOICE, and was conducted in 2 stages: before (stage 1) and after (stage 2) drug detection results were provided to participants. Transcripts from 44 women who participated in both stages were analysed to understand the effect of presenting drug detection data on narratives of product use. Thirty-six women reported high adherence in stage 1, yet admitted non-use in stage 2, three reported high adherence in both stages (contrary to their drug detection results) and five had consistent responses across both stages and drug results. Presenting objective measures of use may facilitate more accurate product use reporting and should be evaluated in future prevention trials.

Abstract access

Editor’s notes: The VOICE trial looked at the effectiveness of PrEP and vaginal microbicides in women in three African countries. One of the findings of the study was low product adherence among some women, based on retrospective drug level testing. In this paper, the authors compare data on product adherence from before and after participants were given plasma drug detection results. The findings are revealing, not least because many of women interviewed explained why they had claimed to be adhering to the drug, when they were not. Women gave many reasons for not being open about taking their medicines/use of the microbicide. It is interesting that a few women continued to say that they were good adherers, even when presented with drug plasma data, which suggested otherwise. This, the authors note, requires further investigation.

The findings provide valuable evidence of the shortcomings of collecting self-reported adherence data. The use of biomedical markers to reveal drug plasma levels is important. However, the qualitative research, which documented the discussion around those findings, is both fascinating and extremely useful. Perhaps in future there will be an even greater willingness to fund good qualitative research as a key component of trials?

Obtaining a male circumcision prevalence rate of 80% among adults in a short time: An observational prospective intervention study in the Orange Farm township of South Africa.

World Health Organization recommends a target for the male circumcision prevalence rate of 80%. This rate will have a substantial impact on the human immunodeficiency virus-acquired immunodeficiency syndrome epidemic in Eastern and Southern Africa. The objective of the study was to assess whether an innovative intervention can lead to an increased voluntary male medical circumcision (VMMC) uptake among adults in a short time. **This prospective observational study of a demand generation intervention was conducted in the township of Orange Farm (South Africa) in August to November 2015.** In this community male circumcision prevalence rate among adults was stable between 2010 and 2015 at 55% and 57%, despite regular VMMC campaigns at community level and the presence of a VMMC clinic that offered free VMMC. The **intervention took place in a random sample of 981 households** where 522 men aged 18 to 49 years accepted to participate in the study. **Among the 226 uncircumcised men, 212 accepted to be enrolled in the intervention study.** A personal male circumcision adviser trained in interpersonal communication skills was assigned to each uncircumcised participant. The **male circumcision advisers were trained to explain the risks and benefits of VMMC, and to discuss 24 possible reasons given by men for not being circumcised.** Participants were then followed for 9 weeks. Each participant had a maximum of 3 motivational interviews at home. Participants who decided to be circumcised received financial compensation for their time equivalent to 2.5 days of work at the minimum **South African salary rate.** Among the 212 uncircumcised men enrolled in the intervention, 69.8% (148/212; 95% confidence interval [CI]; 63.4%-75.7%) **agreed to be circumcised**, which defines the uptake of the intervention. The male circumcision prevalence rate of the sample increased from 56.7% (296/522) to 81.4% (425/522; 77.9%-84.6%), **P < 0.001,** corresponding to a relative increase of 43.6% (95% CI: 35.4%-53.7%). The reported reasons for accepting circumcision were motivational interviews with the male circumcision adviser (83.1%), and time compensation (39.4%). Increased uptake of VMMC uptake can be obtained in a short time among adult males but requires an intense intervention centered on uncircumcised men at an individual level and time compensation.

**Abstract Full-text [free] access**

**Editor’s notes:** As there are diverse motives for and barriers to voluntary male medical circumcision (VMMC), a range of programmes are required to reach WHO’s target of 80% male circumcision. This demand-creation activity study took place in a setting where, following school talks, street animation, flyers and local radio advertising, circumcision prevalence had risen to 57% by 2010 but had then plateaued. The programme was based on the theory that saturation had not been reached and many men who remained uncircumcised were not opposed to it but needed the right opportunity and circumstances to motivate them. In just over two months the prevalence of adult male circumcision in the study sample increased to over 80%, (WHO goal) as a result of implementing up to three home-based motivational interviews, plus time compensation of half a week’s pay at minimum wage for men who had VMMC. Uptake was highest among the oldest men (aged 40-49 years), who had the lowest prevalence of circumcision before the study. Possibly previous programmes that were primarily focussed on adolescents were less likely to affect them. The highest rates were achieved in the youngest age group (aged 18-24 years), who were the most likely to already be circumcised before the study. Time to think about their options at home was important to participants. Most men who opted for VMMC said it was very important to have discussed the situation with their partner (80%) and with relatives or friends (78%). The three motivational interviews produced diminishing yield: 112/212 men sought VMMC after the first interview, 28/78 after the second and 8/54 after the third. After one interview plus financial compensation, the male circumcision prevalence in the sample increased to 75%.
The study is an example of a locally developed and setting-appropriate activity, quickly and rigorously tested in a realistic setting. In this manner, research questions can be relevant to the context and the results can be put into practice.

Could circumcision of HIV-positive males benefit voluntary medical male circumcision programs in Africa? Mathematical modeling analysis.


Background: The epidemiological and programmatic implications of inclusivity of HIV-positive males in voluntary medical male circumcision (VMMC) programs are uncertain. We modeled these implications using Zambia as an illustrative example.

Methods and findings: We used the Age-Structured Mathematical (ASM) model to evaluate, over an intermediate horizon (2010-2025), the effectiveness (number of VMMCs needed to avert one HIV infection) of VMMC scale-up scenarios with varying proportions of HIV-positive males. The model was calibrated by fitting to HIV prevalence time trend data from 1990 to 2014. We assumed that inclusivity of HIV positive males may benefit VMMC programs by increasing VMMC uptake among higher risk males, or by circumcision reducing HIV male-to-female transmission risk. All analyses were generated assuming no further antiretroviral therapy (ART) scale-up. The number of VMMCs needed to avert one HIV infection was projected to increase from 12.2 VMMCs per HIV infection averted, in a program that circumcises only HIV-negative males, to 14.0, in a program that includes HIV-positive males. The proportion of HIV-positive males was based on their representation in the population (e.g. 12.6% of those circumcised in 2010 would be HIV-positive based on HIV prevalence among males of 12.6% in 2010). However, if a program that only reaches out to HIV-negative males is associated with 20% lower uptake among higher-risk males, the effectiveness would be 13.2 VMMCs per infection averted. If improved inclusivity of HIV-positive males is associated with 20% higher uptake among higher-risk males, the effectiveness would be 12.4. As the assumed VMMC efficacy against male-to-female HIV transmission was increased from 0% to 20% and 46%, the effectiveness of circumcising regardless of HIV status improved from 14.0 to 11.5 and 9.1, respectively. The reduction in the HIV incidence rate among females increased accordingly, from 24.7% to 34.8% and 50.4%, respectively.

Conclusion: Improving inclusivity of males in VMMC programs regardless of HIV status increases VMMC effectiveness, if there is moderate increase in VMMC uptake among higher-risk males and/or if there is moderate efficacy for VMMC against male-to-female transmission. In these circumstances, VMMC programs can reduce the HIV incidence rate in males by nearly as much as expected by some ART programs, and additionally, females can benefit from the intervention nearly as much as males.

Abstract Full-text [free] access

Editor's notes: Evidence from randomised control trials and modelling studies suggest that voluntary male medical circumcision (VMMC) is a cost-effective HIV prevention programme. A deterministic compartmental age structured HIV model was used to assess benefits of including HIV positive males in VMMC programmes. The HIV model was parameterized using HIV biological and behavioural data for sub-Saharan Africa. The model was fit to HIV prevalence for Zambia in the years between 1990 and 2014. The model used baseline circumcision coverages from Zambia Demographic and Health Survey 2007. The authors analysed the model for three VMMC programme scenarios; circumcising
HIV negative males only, circumcising both HIV negative and HIV positive males, and circumcising males regardless of their HIV status. Sensitivity analysis was conducted to ascertain the robustness of key model assumptions on the study findings. The findings from the study suggest that, improving the inclusivity of all males is likely to improve the effectiveness of VMMC programmes. This will be the case if there is moderate increase in uptake among higher-risk males and/or moderate VMMC efficacy in preventing male-to-female transmission. This is a very interesting modelling study which gives insights to policymakers on factors to consider in designing VMMC programmes.

3. Key populations

Sexual behaviors and HIV status: a population-based study among older adults in rural South Africa.


Objective: To identify the unmet needs for HIV prevention among older adults in rural South Africa.

Methods: We analyzed data from a population-based sample of 5059 men and women aged 40 years and older from the study Health and Aging in Africa: Longitudinal Studies of INDEPTH Communities (HAALSI), which was carried out in the Agincourt health and sociodemographic surveillance system in the Mpumalanga province of South Africa. We estimated the prevalence of HIV (laboratory-confirmed and self-reported) and key sexual behaviors by age and sex. We compared sexual behavior profiles across HIV status categories with and without age-sex standardization.

Results: HIV prevalence was very high among HAALSI participants (23%, 95% confidence interval [CI]: 21 to 24), with no sex differences. Recent sexual activity was common (56%, 95% CI: 55 to 58) across all HIV status categories. Condom use was low among HIV-negative adults (15%, 95% CI: 14 to 17), higher among HIV-positive adults who were unaware of their HIV status (27%, 95% CI: 22 to 33), and dramatically higher among HIV-positive adults who were aware of their status (75%, 95% CI: 70 to 80). Casual sex and multiple partnerships were reported at moderate levels, with slightly higher estimates among HIV-positive compared to HIV-negative adults. Differences by HIV status remained after age-sex standardization.

Conclusions: Older HIV-positive adults in an HIV hyperendemic community of rural South Africa report sexual behaviors consistent with high HIV transmission risk. Older HIV-negative adults report sexual behaviors consistent with high HIV acquisition risk. Prevention initiatives tailored to the particular prevention needs of older adults are urgently needed to reduce HIV risk in this and similar communities in sub-Saharan Africa.

Abstract Full-text [free] access

Editor’s notes: This large population-based survey was designed to collect data on well-being, health status, cognitive functioning, and aspects of ageing among men and women 40 years of age or older (40+) in Mpumalanga, South Africa. The survey documented an unexpectedly high HIV prevalence of 23% in this age group. In the 50+ age group, almost one in five people (20%) was HIV-positive. This compares to an overall South African national estimate for adults 50 and over in 2012 of 7.6%, the Africa Centre KwaZulu-Natal estimate of 9.5%, and the previous Agincourt estimate of 16.5% in 2010-11. One explanation is that HIV prevalence among older South Africans is climbing as more people access life-prolonging antiretroviral treatment. In addition to this, each year people with
HIV are ageing into the older age group. This study focused on the 40+ age group because life expectancy in the Agincourt study area had been low and collected sexual behaviour information for the previous two-year period, rather than the usual time period of 12 months. Nonetheless, the data obtained through computer-assisted personal interviews reveal ‘recent’ sexual behaviour that both challenges stereotypes that older people are not sexually active and suggests significant risk of HIV transmission and HIV acquisition. Two-thirds reported more than one lifetime sexual partner and although sexual activity did tend to decrease with age, 52% of men and 6% of women aged 80 years and older had been sexually active in the previous two years. Only about half of people found to be HIV-positive knew their status (12%). This group of people living with HIV were far more likely to use condoms. This suggests that an offer of HIV testing in ways that can reach older people would assist in avoiding transmission to partners and in accessing antiretroviral therapy. Only one in seven sexually active HIV-negative people 40+ are using condoms in this setting. This highlights the urgent need for awareness raising to foster new sexual norms to avoid HIV acquisition by practising safer sex. It is time to get our heads out of the sand, recognise the sexuality of older people, and work with them to tailor specific HIV strategies to reduce HIV transmission and acquisition – they too are key to ending AIDS.

Psychiatric symptoms, quality of life, and HIV status among people using opioids in Saint Petersburg, Russia.


Background: The Russian Federation is experiencing a very high rate of HIV infection among people who inject drugs (PWID). However, few studies have explored characteristics of people with co-occurring opioid use disorders and HIV, including psychiatric symptom presentations and how these symptoms might relate to quality of life. The current study therefore explored a.) differences in baseline psychiatric symptoms among HIV+ and HIV- individuals with opioid use disorder seeking naltrexone treatment at two treatment centers in Saint Petersburg, Russia and b.) associations between psychiatric symptom constellations and quality of life.

Methods: Participants were 328 adults enrolling in a randomized clinical trial evaluating outpatient treatments combining naltrexone with different drug counseling models. Psychiatric symptoms and quality of life were assessed using the Brief Symptom Inventory and The World Health Organization Quality of Life-BREF, respectively.

Results: Approximately 60% of participants were HIV+. Those who were HIV+ scored significantly higher on BSI anxiety, depression, psychoticism, somatization, paranoid ideation, phobic anxiety, obsessive-compulsive, and GSI indexes (all p<0.05) than those HIV-. A K-means cluster analysis identified three distinct psychiatric symptom profiles; the proportion of HIV+ was significantly greater and quality of life indicators were significantly lower in the cluster with the highest psychiatric symptom levels.

Conclusion: Higher levels of psychiatric symptoms and lower quality of life indicators among HIV+ (compared to HIV-) individuals injecting drugs support the potential importance of combining interventions that target improving psychiatric symptoms with drug treatment, particularly for HIV+ patients.

Abstract access
Editor’s notes: The higher prevalence of mental health disorders among people living with HIV is well known. This paper focuses on the association of mental health disorders and HIV among people who inject drugs, in St Petersburg, Russian Federation – the city with the highest prevalence of HIV and drug use in the Russian Federation. HIV positive people who inject drugs had significantly higher prevalence of mental health problems than HIV negative people who inject drugs. They had a lower quality of life according to a validated scale, underscoring the need for strong, combination public health programmes to support this vulnerable group. The population studied was selected through existing service provision. Since these individuals were already seeking treatment on their own, there could be many more who are not engaged in care either for HIV treatment or drug use support. This suggests the need to strengthen awareness and services, especially in areas where clean needles and other risk management methods are not yet available.

4. Elimination of gender inequalities


Sex workers in sub-Saharan Africa experience a high burden of HIV with a paucity of data on violence and links to HIV risk among sex workers, and even less within conflict-affected environments. Data are from a cross-sectional survey of female sex workers in Gulu, northern Uganda (n = 400). Logistic regression was used to determine the specific association between policing and recent physical/sexual violence from clients. A total of 196 (49.0%) sex workers experienced physical/sexual violence by a client. From those who experienced client violence the most common forms included physical assault (58.7%), rape (38.3%), and gang rape (15.8%). Police harassment was very common, a total of 149 (37.3%) reported rushing negotiations with clients because of police presence, a practice that was significantly associated with increased odds of client violence (adjusted odds ratio: 1.61, 95% confidence intervals: 1.03-2.52). Inconsistent condom use with clients, servicing clients in a bar, and working for a manager/pimp were also independently associated with recent client violence. Structural and community-led responses, including decriminalisation, and engagement with police and policy stakeholders, remain critical to addressing violence, both a human rights and public health imperative.

Abstract access

Editor’s notes: Sex workers are at increased risk of HIV and of violence from multiple perpetrators. There is a paucity of research examining violence among sex workers in conflict-affected areas. Sex work in Uganda is illegal. A police presence can reduce sex workers ability to screen for dangerous clients, negotiate sex acts, price and condom use. This study is from northern Uganda. The site, now at peace, has experienced 20 years of war. A quarter of sex workers are living with HIV. The paper examines the prevalence of client violence, police arrest and other factors, and how they interrelate.

Participants in the study were usually young (median age 21 years), poorly educated and had ≥1 child. One third had been abducted into the Lord’s Resistance Army and two thirds had lived in an Internal Displacement Camp. Some 49% had experienced recent physical or sexual violence from clients. Eight percent had been gang raped in the past six months. Policing, inconsistent condom use, having sex in a bar and working for a manager or pimp were significantly associated with client
violence. Sex workers in this survey face a high prevalence of violence and HIV. Decriminalisation of sex work is vital if sex workers are to access labour and human rights protection and to reduce the high prevalence of violence and HIV.

5. Elimination of stigma

Another generation of stigma? Assessing healthcare student perceptions of HIV-positive patients in Mwanza, Tanzania.


HIV-related stigma remains a persistent global health concern among people living with HIV/AIDS (PLWA) in developing nations. The literature is lacking in studies about healthcare students’ perceptions of PLWA. This study is the first effort to understand stigmatizing attitudes toward HIV-positive patients by healthcare students in Mwanza, Tanzania, not just those who will be directly treating patients but also those who will be indirectly involved through nonclinical roles, such as handling patient specimens and private health information. A total of 208 students were drawn from Clinical Medicine, Laboratory Sciences, Health Records and Information Management, and Community Health classes at the Tandabui Institute of Health Sciences and Technology for a voluntary survey that assessed stigmatizing beliefs toward PLWA. Students generally obtained high scores on the overall survey instrument, pointing to low stigmatizing beliefs toward PLWA and an overall willingness to treat PLWA with the same standard of care as other patients. However, there are gaps in knowledge that exist among students, such as a comprehensive understanding of all routes of HIV infection. The study also suggests that students who interact with patients as part of their training are less likely to exhibit stigmatizing beliefs toward PLWA. A comprehensive course in HIV infection, one that includes classroom sessions focused on the epidemiology and routes of transmission as well as clinical opportunities to directly interact with PLWA-perhaps through teaching sessions led by PLWA-may allow for significant reductions in stigma toward such patients and improve clinical outcomes for PLWA around the world.

Abstract access

Editor’s notes: This paper reports on a survey of students who were undergoing training in Clinical Medicine, Laboratory Sciences, Health Records and Information Management, Nursing, and Community Health in Mwanza, Tanzania. The survey aimed to explore attitudes about people living with HIV. The authors report that their results illustrate low stigmatizing beliefs towards people living with HIV. However, around a quarter believed that HIV is a punishment for bad behaviour. A third believed that people who acquired HIV from drug use or sex deserved to become infected. Further to this, nearly three quarters believed that individuals who were HIV positive could have avoided infection if they wanted to. A quarter believed that people living with HIV have been promiscuous. There were no differences in response by gender but students under 24 were more likely to have negative attitudes. The authors suggest that this could be due to lower education levels than the older students, although they had not measured this. Students studying Clinical Medicine were less likely to have negative attitudes. On a positive note the students reported that they would treat people living with HIV as equal with other people.
The students displayed some lack of knowledge about routes of HIV infection beyond sex and drug use, especially mother-to-child HIV transmission. The authors suggest that better education in this area may reduce the negative attitudes about people living with HIV, reported by many of the students. Overall, this survey reveals some gaps in education, that if addressed could reduce stigma by health workers against people living with HIV.

6. Health systems and services

Transmission of extensively drug-resistant tuberculosis in South Africa.


Background: Drug-resistant tuberculosis threatens recent gains in the treatment of tuberculosis and human immunodeficiency virus (HIV) infection worldwide. A widespread epidemic of extensively drug-resistant (XDR) tuberculosis is occurring in South Africa, where cases have increased substantially since 2002. The factors driving this rapid increase have not been fully elucidated, but such knowledge is needed to guide public health interventions.

Methods: We conducted a prospective study involving 404 participants in KwaZulu-Natal Province, South Africa, with a diagnosis of XDR tuberculosis between 2011 and 2014. Interviews and medical-record reviews were used to elicit information on the participants' history of tuberculosis and HIV infection, hospitalizations, and social networks. Mycobacterium tuberculosis isolates underwent insertion sequence (IS)6110 restriction-fragment-length polymorphism analysis, targeted gene sequencing, and whole-genome sequencing. We used clinical and genotypic case definitions to calculate the proportion of cases of XDR tuberculosis that were due to inadequate treatment of multidrug-resistant (MDR) tuberculosis (i.e., acquired resistance) versus those that were due to transmission (i.e., transmitted resistance). We used social-network analysis to identify community and hospital locations of transmission.

Results: Of the 404 participants, 311 (77%) had HIV infection; the median CD4+ count was 340 cells per cubic millimeter (interquartile range, 117 to 431). A total of 280 participants (69%) had never received treatment for MDR tuberculosis. Genotypic analysis in 386 participants revealed that 323 (84%) belonged to 1 of 31 clusters. Clusters ranged from 2 to 14 participants, except for 1 large cluster of 212 participants (55%) with a LAM4/KZN strain. Person-to-person or hospital-based epidemiologic links were identified in 123 of 404 participants (30%).

Conclusions: The majority of cases of XDR tuberculosis in KwaZulu-Natal, South Africa, an area with a high tuberculosis burden, were probably due to transmission rather than to inadequate treatment of MDR tuberculosis. These data suggest that control of the epidemic of drug-resistant tuberculosis requires an increased focus on interrupting transmission.

Abstract  Full-text [free] access

Editor’s notes: This paper provides further evidence to support person-to-person transmission being the main driver of the XDR-TB epidemic in KwaZulu-Natal, the most populous province of South Africa. The study combined classical and molecular epidemiology: detailed characterisation of people’s clinical history and social networks alongside genotypic methods to characterise their TB strains. With the most conservative estimate, almost seven in ten XDR-TB cases resulted from
transmission. However, combining the clinical and genotypic information, as many as nine in ten cases may have been attributable to transmission.

So where was transmission happening? This unfortunately was more difficult to answer. Although epidemiological links (mainly at home or at hospitals) could be defined for around one in three cases, many did not share the same TB strain. More detailed understanding of transmission may have been affected by the relatively low coverage of XDR-TB cases by this study. Full information was available for just over one in three laboratory-confirmed XDR-TB cases in the province over the study period. Also, although there was some genetic diversity in the TB strains, there was one dominant strain (LAM4/KZN). This is the strain responsible for the well-characterised clonal outbreak of XDR-TB involving Tugela Ferry.

Most people with XDR-TB in this study were HIV positive. Interestingly, three-quarters of people living with HIV were on ART at the time of their XDR-TB diagnosis, and two-thirds of people had undetectable viral load. This flags up two things. Firstly, it is a reminder that ART alone is unlikely to control the TB (or drug-resistant TB) epidemic in South Africa. Secondly, it raises further questions that could not be definitively answered here as to whether some of these people might have been infected with XDR-TB while accessing HIV treatment and care in the public health system.

So what do we do with this new information? These findings should encourage us to focus on developing strategies to interrupt drug-resistant TB transmission. We need better evidence of what works in community settings and health care settings. We need better evidence of how to deliver proven programmes. We still do not know whether we might need different activities to interrupt MDR- and XDR-TB transmission, or whether this should just be encompassed within broader strategies to interrupt all TB transmission. South Africa is leading the way in implementing molecular diagnostics to help with earlier detection of drug-resistant TB, and is at the forefront of developing and testing new drug regimens for drug-resistant TB. This provides a solid platform on which to develop public health programmes to stop the spread of drug-resistant TB.

Communication about HIV and death: maternal reports of primary school-aged children’s questions after maternal HIV disclosure in rural South Africa.


Introduction: Children's understanding of HIV and death in epidemic regions is under-researched. We investigated children’s death-related questions post maternal HIV-disclosure. Secondary aims examined characteristics associated with death-related questions and consequences for children's mental health.

Methods: HIV-infected mothers (N = 281) were supported to disclose their HIV status to their children (6-10 years) in an uncontrolled pre-post intervention evaluation. Children’s questions post-disclosure were collected by maternal report, 1-2 weeks post-disclosure. 61/281 children asked 88 death-related questions, which were analysed qualitatively. Logistic regression analyses examined characteristics associated with death-related questions. Using the parent-report Child Behaviour Checklist (CBCL), linear regression analysis examined differences in total CBCL problems by group, controlling for baseline.

Results: Children's questions were grouped into three themes: 'threats'; 'implications' and 'clarifications'. Children were most concerned about the threat of death, mother’s survival, and prior family deaths. In multivariate analysis variables significantly associated with asking death-related questions included an absence of regular remittance to the mother (AOR 0.25 [CI 0.10, 0.59] p
= 0.002), mother reporting the child's initial reaction to disclosure being "frightened" (AOR 6.57 [CI 2.75, 15.70] p≤0.001) and level of disclosure (full/partial) to the child (AOR 2.55 [CI 1.28, 5.06] p = 0.008). Controlling for significant variables and baseline, all children showed improvements on the CBCL post-intervention; with no significant differences on total problems scores post-intervention (β -0.096 SE1.366 t = -0.07 p = 0.944).

Discussion: The content of questions children asked following disclosure indicate some understanding of HIV and, for almost a third of children, its potential consequence for parental death. Level of maternal disclosure and stability of financial support to the family may facilitate or inhibit discussions about death post-disclosure. Communication about death did not have immediate negative consequences on child behaviour according to maternal report.

Conclusion: In sub-Saharan Africa, given exposure to death at young ages, meeting children's informational needs could increase their resilience.

Abstract Full-text [free] access

Editor’s notes: This is an unusual study examining the experience of the disclosure conversation between mother and child about the mother’s HIV positive status in Kwazulu-Natal. The paper examines the death-associated questions that mothers reported children (aged 6-10 years old, HIV exposed but uninfected) asked up to one week after the ‘disclosure event’. The findings indicate that although the treatability and chronic nature of HIV is complex, children's questions suggest that they are attempting understand the implications of their mother’s HIV positive status for them, their mother’s and their care. Much research has illustrated that disclosure of both the parents or the child's own HIV positive status is commonly delayed. This delay may exacerbate the challenges a young person has in adapting to this knowledge. We also know that parents, like a large proportion of people living with HIV, are daunted and feel ill equipped to manage disclosure to others, especially children. However little evidence is currently available evaluating the impact of programmes that are designed to support parents to disclose their own HIV status to their children. Therefore, this programme and study is very welcome.

The focus on death-questions is particularly interesting. This provides some illustration of how children are reportedly processing the information that they have been given. Many questions indicate a prior knowledge of HIV, illness and/ or death. It also suggests that children are managing this new knowledge within this broader context. Within this high HIV-prevalence context, a discursive emphasis on the efficacy of HIV treatment to reduce the risk of HIV-associated mortality within the delivery of timely, age-appropriate education information may be critical. This can reduce fears around maternal death and supporting children to manage and adapt to their situations. A clear direction for further enquiry would be to follow up these families to assess the impact of full/ partial disclosure over time on the children and the mothers.

Effect of new tuberculosis diagnostic technologies on community-based intensified case finding: a multicentre randomised controlled trial.


Background: Inadequate case detection results in high levels of undiagnosed tuberculosis in sub-Saharan Africa. Data for the effect of new diagnostic tools when used for community-based intensified case finding are not available, so we investigated whether the use of sputum
Xpert®-MTB/RIF and the Determine™ TB LAM urine test in two African communities could be effective.

Methods: In a pragmatic, randomised, parallel-group trial with individual randomisation stratified by country, we compared sputum Xpert®-MTB/RIF, and if HIV-infected, the Determine™ TB LAM urine test (novel diagnostic group), with laboratory-based sputum smear microscopy (routine diagnostic group) for intensified case finding in communities with high tuberculosis and HIV prevalence in Cape Town, South Africa, and Harare, Zimbabwe. Participants were randomly assigned (1:1) to these groups with computer-generated allocation lists, using culture as the reference standard. In Cape Town, participants were randomised and tested at an Xpert®-equipped mobile van, while in Harare, participants were driven to a local clinic where the same diagnostic tests were done. The primary endpoint was the proportion of culture-positive tuberculosis cases initiating tuberculosis treatment in each study group at 60 days. This trial is registered at ClinicalTrials.gov, number NCT01990274.

Findings: Between Oct 18, 2013, and March 31, 2015, 2261 individuals were screened and 875 (39%) of these met the criteria for diagnostic testing. 439 participants were randomly assigned to the novel group and 436 to the routine group. 74 (9%) of 875 participants had confirmed tuberculosis. If late culture-based treatment initiation was excluded, more patients with culture-positive tuberculosis were initiated on treatment in the novel group at 60 days (36 [86%] of 42 in the novel group vs 18 [56%] of 32 in the routine group). Thus the difference in the proportion initiating treatment between groups was 29% (95% CI 9-50, p=0.0047) and 53% more patients initiated therapy in the novel diagnostic group than in the routine diagnostic group. One culture-positive patient was treated based only on a positive LAM test.

Interpretation: Compared with traditional tools, Xpert®-MTB/RIF for community-based intensified case finding in HIV and tuberculosis-endemic settings increased the proportion of patients initiating treatment. By contrast, urine LAM testing was not found to be useful for intensive case finding in this setting.

Abstract access

Editor’s notes: Undiagnosed tuberculosis (TB) is the main source of ongoing transmission of Mycobacterium tuberculosis in the community. Community-based intensified TB case finding strategies in high prevalence settings aim to reduce the prevalence of undiagnosed tuberculosis (TB) and thereby to reduce TB transmission. This is the first randomised trial to date comparing a point of contact diagnostic tool, Xpert® MTB/RIF, with a traditional tool, smear microscopy, for community-based intensive case-finding in sub-Saharan Africa.

The key finding was that a community-based intensified strategy using Xpert® MTB/RIF reduced time-to-treatment and increased the proportion of culture-positive people started on treatment in the first 60 days (when culture-based treatment initiation was not included). Additional findings included a reduction in the number of people with TB treated empirically and a 50% increase in 60-day detection rate compared with smear microscopy. However, there was no difference by study arm in the proportion of culture-positive people who were retained on TB treatment at six months, and this was suboptimal (69% versus 71% for routine versus novel). The study also demonstrated that it was feasible to undertake community-based screening by minimally trained health-care workers using Xpert® in a mobile van with a generator or on site within a community-based clinic.

It is interesting to note that there were major differences between study sites. In multivariable analysis, study site was the strongest risk factor for a shorter time-to-treatment initiation among
culture-positive cases (Harare versus Cape Town - adjusted hazard ratio 7.18, 95% confidence interval 3.69 – 13.96) with screening method (novel versus routine diagnostics) found to have an adjusted hazard ratio of 2.32 (95% confidence interval 1.35 – 3.97). This finding likely reflects differences in the clinical management of Xpert®-negative and smear-negative people with presumed TB between study sites. In Harare, almost all people with a negative test result (in either arm) were referred for chest radiography, and probably because of this, a much larger proportion of study participants were started on anti-tuberculosis treatment in Harare compared to Cape Town (49% versus 9%). There was also a major difference in retention on treatment at six months among culture-positive people (81% in Harare versus 59% in Cape Town). These results highlight the importance of context, including heterogeneity in patient characteristics and differences in quality of health-care, access and practices between settings, in interpreting study findings associated with TB case-finding strategies.

Whether implementation of community-based intensive case finding using Xpert® in high-prevalence areas actually translates into reduced community TB transmission or improved clinical outcomes remains to be determined.

Prevalence of anal HPV and anal dysplasia in HIV-infected women from Johannesburg, South Africa.


Background: Anal cancer is a relatively common cancer among HIV-infected populations. There are limited data on the prevalence of anal high-risk human papillomavirus (HR-HPV) infection and anal dysplasia in HIV-infected women from resource-constrained settings.

Methods: A cross-sectional study of HIV-infected women age 25-65 recruited from an HIV clinic in Johannesburg, South Africa. Cervical and anal swabs were taken for conventional cytology and HR-HPV testing. Women with abnormal anal cytology and 20% of women with negative cytology were seen for high resolution anoscopy (HRA) with biopsy of visible lesions.

Results: Two hundred women were enrolled. Anal HR-HPV was found in 43%. The anal cytology results were negative in 51 (26%); 97 (49%) had low-grade squamous intraepithelial lesions (SIL), 32 (16%) had atypical squamous cells of unknown significance and 19 (9.5%) had high-grade SIL or atypical squamous cells suggestive of high-grade SIL. On HRA, 71 (36%) had atypia or low-grade SIL on anal histology and 17 (8.5%) had high-grade SIL. Overall 31 (17.5%) had high-grade SIL present on anal cytology or histology. Abnormal cervical cytology was found in 70% and cervical HR-HPV in 41%.

Conclusion: We found a significant burden of anal HR-HPV infection, abnormal anal cytology and high-grade SIL in our cohort. This is the first study of the prevalence of anal dysplasia in HIV-infected women from sub-Saharan Africa. Additional studies are needed to define the epidemiology of these conditions, as well as the incidence of anal cancer, in this population.

Abstract access

Editor’s notes: Women living with HIV have a higher incidence of anogenital cancers compared to HIV-negative women, even in the ART era. Previous studies have illustrated that women living with HIV in South Africa have a high risk of cervical high-risk (HR)-HPV, and high rates of high-grade
cervical intraepithelial neoplasia. This is the first study to report the prevalence of anal HR-HPV and anal high-grade squamous intraepithelial lesions (HSIL+) among women living with HIV in Africa.

This cross-sectional study among 200 women living with HIV attending a HIV treatment centre in Johannesburg, South Africa, the majority (97%) of whom were on ART, reported a high prevalence of anal HR-HPV and anal HSIL+ by high-resolution anoscopy (43% and 8.5%, respectively). Women with low current CD4+ cell count and with shorter duration of ART use had marginally higher prevalence of anal HR-HPV and HSIL+.

It remains unclear whether high-grade anal lesions among women living with HIV have the same propensity to progress to anal cancer as is known to occur for high-grade cervical lesions to cervical cancer. Studies among HIV-positive and HIV-negative men report frequent spontaneous regression of anal intraepithelial lesions (AIN) and high rates of recurrence following treatment, but longitudinal data are limited among women living with HIV. Prolonged ART use may have contributed to a reduction in HPV-associated cervical lesions, and the same could be true for anal lesions. Larger prospective studies are necessary to define the rates of high-grade lesion incidence and progression and associated risk factors among women living with HIV in order to guide screening and management decisions.