Welcome to the 7th issue of HIV this month! In this issue, we cover the following topics:

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

Technology is advancing rapidly, but are we making the most of it?

Editor’s notes: HIV self-testing was a key area of discussion in the Paris IAS meeting. UNITAID signed the next phase of the STAR Initiative that is working with six countries in Southern Africa to transform the market for self-testing and understand the impact of different delivery systems. The Bill and Melinda Gates Foundation are using their resources to lower prices of self-test kits. Following WHO’s decision to prequalify an oral fluid test, many countries are including self-test commodities within their PEPFAR Country Operation Plans and Global Fund concept notes. WHO have issued guidance on self-testing and assisted partner notification. So we can expect to see more and more self-tests out there in the field!

In Malawi, Choko et al. reported on qualitative research done prior to a cluster randomized trial that involves providing self-tests to women attending antenatal care (ANC) for them to take home to their partners. Although couples are welcomed at ANC clinics and couple testing is certainly beneficial, many men still feel that the clinic is not a place for them. As one participant said: “Considering what happens here at the ANC clinic, I don’t see my husband escorting me anymore because you find he is alone among many women and he has to listen to some things concerning birth. . . .”

In contrast, many women and men engaged in conversations about how providing self-test kits could help communication, stigma, privacy, control and time pressure among other aspects of involving men in HIV testing. Some concerns were raised around violence and it is clear that this approach will suit some but not all couples, so it needs to be delivered in a way that respects autonomy with no coercion.

In a very different context, Jamil et al. have conducted a randomized trial among Australian gay men and men who have sex with men. The trial enrolled “high risk” men who reported multiple partners and condomless sex over the past months. A central premise of public health strategies to control the HIV epidemic is to find people who have acquired HIV as early as possible. So the trial aimed to determine whether the offer of free oral fluid self-tests led to earlier testing and more frequent testing. They found that compared with standard care, availability of free oral-fluid self-testing increased testing frequency both in men who had not tested recently and in men who had not tested at all in the past years. Importantly there was no decline in facility-based testing for HIV or sexually transmitted infections, which might have implied replacement. The men commented that self-testing was highly acceptable and easy to do.

Self-tests are not a panacea. Oral fluid tests do have a slightly lower sensitivity than blood based tests. This may be important when HIV-antibody levels are not high, particularly in people taking ART (either as treatment or as PrEP), or early in the course of infection. Furthermore, both oral fluid and blood based test rely on visual identification of bands on the test strip that may be faint, leading to some people assuming that they are negative or failing to see the positive band. Curlin et al. examined the performance of oral fluid tests in people seroconverting to HIV during three specific trials. They found a considerable number of false negative results and a long delay before some individuals became positive on oral fluid tests. There was also a clear suggestion that some test operators were less good than others at performing the test and the possibility that one batch of the test kits were less sensitive. Overall they concluded that “caution must be exercised when interpreting a negative oral fluid test in settings where acute infection is likely, and where PrEP use, ART induced viral suppression, or profound immunosuppression may result in low HIV-specific antibody titers.” However, as an additional screening tool to be used in populations where many of whom are “missing” from the first 90 are to be found, self-tests have much to offer. Many of these
people will have acquired HIV some time ago and by definition will not be taking ART. So the cautions raised by Curlin et al. may be less relevant for the primary intended purpose of self-tests. Nonetheless, they make it very clear that oral fluid self-tests are not an appropriate technology to follow people on treatment or on PrEP. Nor are they recommended for the diagnosis of acute infection.

While self-tests may increase the proportion of adults knowing their HIV status, different technology is needed for infants. Nucleic acid amplification is used to detect pro-viral DNA or viral RNA in samples from infants. The technology is more complex and often centralized, leading to delays and loss to follow up in mother-infant pairs. Several systems now aim to provide testing close to the point of care and the evaluation of the SAMBA HIV-1 Qual Whole Blood Test from Ondiek et al. is an encouraging report. Sensitivity and specificity were high (98.5% and 99.8% on 745 infant samples) and comparable to the standard approach used in centralized labs. Samples from those with discrepant results were rechecked by assays based on multiple targets and suggested that the SAMBA test and the standard approach were each responsible for some of the few false positive and negatives seen. The advantages of the SAMBA system is that it has been designed to be used in peripheral health systems. All the reagents are freeze dried and stable without refrigeration. Turnaround time is approximately 2 hours with minimal sample handling once the sample is put into the machine. Costs will still need to come down, but competition with other manufacturers may help.

The SAMBA technology that was evaluated is a qualitative assay aimed at diagnosis of infants. A larger market is for viral load assays that are central to the monitoring of the effectiveness of HIV treatment and form the indicator for UNAIDS’s third 90. However, at the moment viral load assays are still too expensive. As a result the optimal strategy for their use remains uncertain within programmes that have to make difficult decisions about where their limited resources should be spent.

Negoescu et al. have built an interesting model to explore the economic trade-offs between different frequencies of performing viral load assays. More importantly they explore models of adapting the frequency of assays according to characteristics of the person taking ART. People who have been on treatment for longer periods, or are older, or report fewer problems with adherence could be selected for less frequent assays. This could save resources, without compromising health outcomes. However, for countries like Uganda, which was used as the example to calibrate the model, the best approach seems to still be a viral load assay once per year, regardless of other factors. And indeed, many resource limited countries are having to make difficult choices about how to allocate stretched budgets between expansion of access to viral load assays to the possible detriment of basic prevention programmes such as male circumcision and condoms. As more resources become available (or as the cost of viral load assays fall) countries may well choose to do more frequent viral load assays. The authors showed that monthly assays were more expensive but did (unsurprisingly) lead to benefits in terms of earlier detection of virological failure. Given the renewed attention to drug resistance and the role of late detection of HIV treatment failure in propagating it, such models may become increasingly important. Adapting the viral load assay frequency to the characteristics of the person taking HIV treatment could be a sensible approach in middle and higher income settings.

For some years, WHO has recommended that nucleic acid amplification should also be used as the first line test for tuberculosis among people living with HIV. The GeneXpert® system has been taken up quite widely in many countries where HIV is common among people with tuberculosis, most notably in South Africa. However, Hermans et al. remind us that technology is only one part of the solution. Although there is no doubt that Xpert™ is considerably more sensitive than sputum microscopy and considerably quicker than mycobacterial culture, incorporating the technology into
routine practice is not always straightforward. At the Infectious Disease Institute in Kampala, Uganda, where there are well trained clinicians and better resources than in much of the rest of Uganda, Xpert™ was made available at no cost for the diagnosis of tuberculosis in a one stop combined HIV-TB clinic. In a cohort of people living with HIV with symptoms suggestive of possible tuberculosis and whose sputum smear microscopy result was negative, many clinicians still preferred to treat on the basis of their clinical judgement and chest radiography. Xpert™ was requested in less than half the patients. Similar numbers of people were started on treatment for tuberculosis regardless of whether Xpert™ was requested (22% vs 21%). And among those in whom an Xpert™ was performed, more were started on anti-tuberculosis treatment who had had a negative test than a positive one. So it was not really clear that Xpert™ was useful in the diagnosis and management of HIV-related tuberculosis in this setting. Xpert™ is not 100% sensitive, so many clinicians will choose to treat patients who might have tuberculosis regardless of the results of new technology. Xpert™ also give a result that includes resistance to rifampicin, but this was not such a major issue in Kampala and was not an objective of this study. Those treated without a confirmed test result were more likely to die during the next 12 months, but the authors point out that there are many possible reasons for this. Many clinicians are aware of the high rates of undiagnosed tuberculosis found at autopsy in people with HIV. Thus, empirical treatment is often given to those who are critically unwell, even when there is no clear evidence of tuberculosis.

GeneXpert® was also the technology used in another study of tuberculosis contact tracing among school children in Swaziland (Ustero et al.). Despite a rapid and extensive response to look for additional cases in schools where a confirmed case of tuberculosis had been found, no secondary cases were identified. In household contacts of the same children, they found an additional two cases. WHO recommends contacts tracing in households of infectious tuberculosis patients. Although there is still a large and important gap in the estimated number of tuberculosis cases and the number who are notified and treated by national programmes, the best ways to find the missing cases are not well established. Even in settings where both infections are among the most important causes of mortality, tuberculosis is much less prevalent than HIV. So the challenge for case-finding and screening approaches for tuberculosis is to select the populations most at risk. An alternative would be to develop tools that are so sensitive, specific and cheap that they can be used for widespread screening. GeneXpert® is not that tool.

While tuberculosis remains the single most important cause of mortality among people living with HIV in low resource settings, there is welcome and increasing attention being paid to human papillomaviruses (HPV). Certain types of HPV are the cause of cervical cancer. This is an AIDS-defining illness both because it is more common among women living with HIV and because it has such a high mortality when only detected at the late stages. At the Paris conference there was a morning session on how to do more about cervical cancer and in particular how to build on the synergies of both HPV and HIV programmes to provide more integrated services for women who are at risk of both infections. The most important types of HPV that cause cervical cancer can be prevented by vaccination. However, to be most effective the vaccine has to be given prior to becoming infected with the relevant HPV strain. So the study by Sudenga et al. in South Africa is useful as it demonstrates how many younger women aged 16-24 years in the Western Cape Province had antibodies against four of the important types included in the quadrivalent vaccine that they were testing. The majority of participants (64%) had antibodies to two or more types present at enrolment and 12% had antibodies to all four. Furthermore, among those participants who received placebo injections, the seroconversion rates were alarming high at 23% for HPV16 and 5% for HPV6 over the 7 months of the study among baseline seronegative participants. South Africa has been a leader in the region in HPV vaccination for schoolgirls. It is clear that vaccination needs to happen at a young
enough age to catch most girls before they become sexually active. This is in contrast to the offer of pre-exposure prophylaxis, which should be focused on young women who are already sexually active and at higher risk of acquiring HIV. The specificities of synergies and integration need to be clearly delineated if we are to maximize efficiency.

HPV is also the principal cause of anal carcinoma, which is a significant problem among gay men and men who have sex with men. Jin et al. have been building on the progress in cervical cancer screening, where new technologies such as nucleic acid detection or oncoprotein detection are leading to big improvements in some settings and replacing cytology as the first line screen for women. The authors determined whether similar biomarkers including both nucleic acids and cellular markers could be used instead of anal cytology. As with most advances in diagnostic technology, there is a trade-off between sensitivity and specificity. Tests that do not miss any cases of neoplastic change are also likely to lead to many people being unnecessarily referred for further assessment and treatment. However, both new approaches seem to be able to be calibrated in this Australian population to allow fewer referrals while still maintaining a similar sensitivity to the current cytological approach.

Acceptability of woman-delivered HIV self-testing to the male partner, and additional interventions: a qualitative study of antenatal care participants in Malawi.


Introduction: In the era of ambitious HIV targets, novel HIV testing models are required for hard-to-reach groups such as men, who remain underserved by existing services. Pregnancy presents a unique opportunity for partners to test for HIV, as many pregnant women will attend antenatal care (ANC). We describe the views of pregnant women and their male partners on HIV self-test kits that are woman-delivered, alone or with an additional intervention.

Methods: A formative qualitative study to inform the design of a multi-arm multi-stage cluster-randomized trial, comprised of six focus group discussions and 20 in-depth interviews, was conducted. ANC attendees were purposively sampled on the day of initial clinic visit, while men were recruited after obtaining their contact information from their female partners. Data were analysed using content analysis, and our interpretation is hypothetical as participants were not offered self-test kits.

Results: Providing HIV self-test kits to pregnant women to deliver to their male partners was highly acceptable to both women and men. Men preferred this approach compared with standard facility-based testing, as self-testing fits into their lifestyles which were characterized by extreme day-to-day economic pressures, including the need to raise money for food for their household daily. Men and women emphasized the need for careful communication before and after collection of the self-test kits in order to minimize the potential for intimate partner violence although physical violence was perceived as less likely to occur. Most men stated a preference to first self-test alone, followed by testing as a couple. Regarding interventions for optimizing linkage following self-testing, both men and women felt that a fixed financial incentive of approximately USD$2 would increase linkage. However, there were concerns that financial incentives of greater value may lead to multiple pregnancies and lack of child spacing. In this low-income setting, a lottery incentive was considered overly disappointing for those who receive nothing. Phone call reminders were preferred to short messaging service.
Conclusions: Woman-delivered HIV self-testing through ANC was acceptable to pregnant women and their male partners. Feedback on additional linkage enablers will be used to alter pre-planned trial arms.

Abstract  Full-text [free] access

Effect of availability of HIV self-testing on HIV testing frequency in gay and bisexual men at high risk of infection (FORTH): a waiting-list randomised controlled trial.


Background: Frequent testing of individuals at high risk of HIV is central to current prevention strategies. We aimed to determine if HIV self-testing would increase frequency of testing in high-risk gay and bisexual men, with a particular focus on men who delayed testing or had never been tested before.

Methods: In this randomised trial, HIV-negative high-risk gay and bisexual men who reported condomless anal intercourse or more than five male sexual partners in the past 3 months were recruited at three clinical and two community-based sites in Australia. Enrolled participants were randomly assigned (1:1) to the intervention (free HIV self-testing plus facility-based testing) or standard care (facility-based testing only). Participants completed a brief online questionnaire every 3 months, which collected the number of self-tests used and the number and location of facility-based tests, and HIV testing was subsequently sourced from clinical records. The primary outcome of number of HIV tests over 12 months was assessed overall and in two strata: recent (last test ≤2 years ago) and non-recent (>2 years ago or never tested) testers. A statistician who was masked to group allocation analysed the data; analyses included all participants who completed at least one follow-up questionnaire. After the 12 month follow-up, men in the standard care group were offered free self-testing kits for a year. This trial is registered with the Australian New Zealand clinical trials registry, number actrn12613001236785.

Findings: Between Dec 1, 2013, and Feb 5, 2015, 182 men were randomly assigned to self-testing, and 180 to standard care. The analysis population included 178 (98%) men in the self-testing group (174 person-years) and 165 (92%) in the standard care group (162 person-years). Overall, men in the self-testing group had 701 HIV tests (410 self-tests; mean 4·0 tests per year), and men in the standard care group had 313 HIV tests (mean 1·9 tests per year); rate ratio (rr) 2·08 (95% ci 1·82-2·38; p<0·0001). Among recent testers, men in the self-testing group had 627 tests (356 self-tests; mean 4·2 per year), and men in the standard care group had 297 tests (mean 2·1 per year); rr 1·99 (1·73-2·29; p<0·0001). Among non-recent testers, men in the self-testing group had 74 tests (54 self-tests; mean 2·8 per year), and men in the standard care group had 16 tests (mean 0·7 per year); rr 3·95 (2·30-6·78; p<0·0001). The mean number of facility-based HIV tests per year was similar in the self-testing and standard care groups (mean 1·7 vs 1·9 per year, respectively; rr 0·86, 0·74-1·01; P=0·074). No serious adverse events were reported during follow-up.

Interpretation: HIV self-testing resulted in a two times increase in frequency of testing in gay and bisexual men at high risk of infection, and a nearly four times increase in non-recent testers, compared with standard care, without reducing the frequency of facility-based HIV testing. HIV self-testing should be made more widely available to help increase testing and earlier diagnosis.
Abstract access

Analysis of false-negative human immunodeficiency virus rapid tests performed on oral fluid in 3 international clinical research studies.


Background: The OraQuick Advance Rapid HIV-1/2 Test is a point-of-care test capable of detecting human immunodeficiency virus (HIV)-specific antibodies in blood and oral fluid. To understand test performance and factors contributing to false-negative results in longitudinal studies, we examined results of participants enrolled in the Botswana TDF/FTC Oral HIV Prophylaxis Trial, the Bangkok Tenofovir Study, and the Bangkok MSM Cohort Study, 3 separate clinical studies of high-risk, HIV-negative persons conducted in Botswana and Thailand.

Methods: In a retrospective observational analysis, we compared oral fluid OraQuick (OFOQ) results among participants becoming HIV infected to results obtained retrospectively using enzyme immunoassay and nucleic acid amplification tests on stored specimens. We categorized negative OFOQ results as true-negative or false-negative relative to nucleic acid amplification test and/or enzyme immunoassay, and determined the delay in OFOQ conversion relative to the estimated time of infection. We used log-binomial regression and generalized estimating equations to examine the association between false-negative results and participant, clinical, and testing-site factors.

Results: Two-hundred thirty-three false-negative OFOQ results occurred in 80 of 287 seroconverting individuals. Estimated OFOQ conversion delay ranged from 14.5 to 547.5 (median, 98.5) days. Delayed OFOQ conversion was associated with clinical site and test operator (P < .05), preexposure prophylaxis (P = .01), low plasma viral load (P < .02), and time to kit expiration (P < .01). Participant age, sex, and HIV subtype were not associated with false-negative results. Long OFOQ conversion delay time was associated with antiretroviral exposure and low plasma viral load.

Conclusions: Failure of OFOQ to detect HIV-1 infection was frequent and multifactorial in origin. In longitudinal trials, negative oral fluid results should be confirmed via testing of blood samples.

Abstract access

Multi-country validation of SAMBA - A novel molecular point-of-care test for HIV-1 detection in resource-limited setting.


Introduction: Early diagnosis of HIV-1 infection and the prompt initiation of antiretroviral therapy are critical to achieving a reduction in the morbidity and mortality of infected infants. The SAMBA HIV-1 Qual Whole Blood Test was developed specifically for early infant diagnosis and prevention of mother-to-child transmission programs implemented at the point-of-care in resource-limited settings.
Methods: We have evaluated the performance of this test run on the SAMBA I semi-automated platform with fresh whole blood specimens collected from 202 adults and 745 infants in Kenya, Uganda, and Zimbabwe. Results were compared with those obtained with the Roche COBAS AmpliPrep/COBAS TaqMan (CAP/CTM) HIV-1 assay as performed with fresh whole blood or dried blood spots of the same subjects, and discrepancies were resolved with alternative assays.

Results: The performance of the SAMBA and CAP/CTM assays evaluated at five laboratories in the three countries was similar for both adult and infant samples. The clinical sensitivity, specificity, and positive and negative predictive values for the SAMBA test were 100%, 99.2%, 98.7%, and 100%, respectively, with adult samples, and 98.5%, 99.8%, 99.7%, and 98.8%, respectively, with infant samples.

Discussion: Our data suggest that the SAMBA HIV-1 Qual Whole Blood Test would be effective for early diagnosis of HIV-1 infection in infants at point-of-care settings in sub-Saharan Africa.

Abstract access

Differentiated human immunodeficiency virus RNA monitoring in resource-limited settings: an economic analysis.


Background: Viral load (VL) monitoring for patients receiving antiretroviral therapy (ART) is recommended worldwide. However, the costs of frequent monitoring are a barrier to implementation in resource-limited settings. The extent to which personalized monitoring frequencies may be cost-effective is unknown.

Methods: We created a simulation model parameterized using person-level longitudinal data to assess the benefits of flexible monitoring frequencies. Our data-driven model tracked human immunodeficiency virus (HIV)-infected individuals for 10 years following ART initiation. We optimized the interval between viral load tests as a function of patients’ age, gender, education, duration since ART initiation, adherence behavior, and the cost-effectiveness threshold. We compared the cost-effectiveness of the personalized monitoring strategies to fixed monitoring intervals every 1, 3, 6, 12, and 24 months.

Results: Shorter fixed VL monitoring intervals yielded increasing benefits (6.034 to 6.221 discounted quality-adjusted life-years [QALYs] per patient with monitoring every 24 to 1 month over 10 years, respectively, standard error = 0.005 QALY), at increasing average costs: US$3445 (annual monitoring) to US$5393 (monthly monitoring) per patient, respectively (standard error = US$3.7). The adaptive policy optimized for low-income contexts achieved 6.142 average QALYs at a cost of US$3524, similar to the fixed 12-month policy (6.135 QALYs, US$3518). The adaptive policy optimized for middle-income resource settings yields 0.008 fewer QALYs per person, but saves US$204 compared to monitoring every 3 months.

Conclusions: The benefits from implementing adaptive vs fixed VL monitoring policies increase with the availability of resources. In low- and middle-income countries, adaptive policies achieve similar outcomes to simpler, fixed-interval policies.

Abstract Full-text [free] access
Treatment decisions and mortality in HIV-positive presumptive smear-negative TB in the Xpert™ MTB/RIF era: a cohort study.


Background: The Xpert™ MTB/RIF (XP) has a higher sensitivity than sputum smear microscopy (70% versus 35%) for TB diagnosis and has been endorsed by the WHO for TB high burden countries to increase case finding among HIV co-infected presumptive TB patients. Its impact on the diagnosis of smear-negative TB in a routine care setting is unclear. We determined the change in diagnosis, treatment and mortality of smear-negative presumptive TB with routine use of Xpert™ MTB/RIF (XP).

Methods: Prospective cohort study of HIV-positive smear-negative presumptive TB patients during a 12-month period after XP implementation in a well-staffed and trained integrated TB/HIV clinic in Kampala, Uganda. Prior to testing clinicians were asked to decide whether they would treat empirically prior to Xpert™ result; actual treatment was decided upon receipt of the XP result. We compared empirical and XP-informed treatment decisions and all-cause mortality in the first year.

Results: Of 411 smear-negative presumptive TB patients, 175 (43%) received an XP; their baseline characteristics did not differ. XP positivity was similar in patients with a pre-XP empirical diagnosis and those without (9/29 [17%] versus 14/142 [10%], P = 0.23). Despite XP testing high levels of empirical treatment prevailed (18%), although XP results did change who ultimately was treated for TB. When adjusted for CD4 count, empirical treatment was not associated with higher mortality compared to no or microbiologically confirmed treatment.

Conclusions: XP usage was lower than expected. The lower sensitivity of XP in smear-negative HIV-positive patients led experienced clinicians to use XP as a "rule-in" rather than "rule-out" test, with the majority of patients still treated empirically.

Abstract  Full-text [free] access

School and household tuberculosis contact investigations in Swaziland: Active TB case finding in a high HIV/TB burden setting.


Background: Investigation of household contacts exposed to infectious tuberculosis (TB) is widely recommended by international guidelines to identify secondary cases of TB and limit spread. There is little data to guide the use of contact investigations outside of the household, despite strong evidence that most TB infections occur outside of the home in TB high burden settings. In older adolescents, the majority of infections are estimated to occur in school. Therefore, as part of a project to increase active case finding in Swaziland, we performed school contact investigations following the identification of a student with infectious TB.

Methods: The Butimba Project identified 7 adolescent TB index cases (age 10-20) with microbiologically confirmed disease attending 6 different schools between June 2014 and March 2015. In addition to household contact investigations, Butimba Project staff worked with the Swaziland School Health Programme (SHP) to perform school contact investigations. At 6 school TB
screening events, between May and October 2015, selected students underwent voluntary TB screening and those with positive symptom screens provided sputum for TB testing.

Results: Among 2015 student contacts tested, 177 (9%) screened positive for TB symptoms, 132 (75%) produced a sputum sample, of which zero tested positive for TB. Household contact investigations of the same index cases yielded 40 contacts; 24 (60%) screened positive for symptoms; 19 produced a sputum sample, of which one case was confirmed positive for TB. The odds ratio of developing TB following household vs. school contact exposure was significantly lower (OR 0.0, 95% CI 0.0 to 0.18, P = 0.02) after exposure in school.

Conclusion: School-based contact investigations require further research to establish best practices in TB high burden settings. In this case, a symptom-based screening approach did not identify additional cases of tuberculosis. In comparison, household contact investigations yielded a higher percentage of contacts with positive TB screens and an additional tuberculosis case.

Abstract Full-text [free] access

HPV serostatus pre- and post-vaccination in a randomized phase II preparedness trial among young Western Cape, South African women: the EVRI trial.


Background: HPV antibodies are a marker of past exposure to the virus. Our objective was to assess HPV serostatus pre- and post-vaccination among HIV-negative women.

Methods: Women aged 16-24 years old were randomized in a placebo controlled trial utilizing the 4-valent HPV (4vHPV) vaccine (NCT01489527, clinicaltrials.gov). Participants (n=389) received the 4vHPV vaccine or placebo following a three dose schedule. Sera were collected at Day 1 and Month 7 for assessment of HPV 6, 11, 16, and 18 neutralizing antibody levels using a multiplex competitive Luminex immunoassay (Merck) based on detecting the L1 capsid antigen for each HPV type.

Results: Seroprevalence was 73% for HPV6, 47% for HPV11, 33% for HPV16, and 44% for HPV18. Seroprevalence for any HPV type did not significantly differ by age or lifetime number of partners. The majority of participants (64%) had two or more 4vHPV antibodies present at enrollment and 12% had antibodies to all four. Among women in the vaccine arm, those that were seropositive for HPV16 at enrollment had higher titers at month 7 compared to women that were seronegative for HPV16 at enrollment; this trend holds for the other HPV types as well. Seroconversion among baseline seronegative participants in the placebo group ranged from 5% for HPV16 to 23% for HPV6.

Conclusion: HPV seroprevalence was high in this population, emphasizing the need to vaccinate prior to sexual debut.

Abstract access

The performance of human papillomavirus biomarkers in predicting anal high-grade squamous intraepithelial lesions in gay and bisexual men.
Background: We evaluate the performance of human papillomavirus (HPV) biomarkers in prediction of anal histological high-grade squamous intraepithelial lesions in gay and bisexual men (GBM) in Sydney, Australia.

Design: Baseline analysis of a 3-year cohort study.

Methods: The study of the prevention of anal cancer is a natural history study of anal HPV infection in GBM aged at least 35 years. All participants completed cytological and histological assessments. Stored ThinPrep PreservCyt residua were tested for HPV genotyping (Linear Array and Cobas 4800) and viral load, E6/E7 mRNA expression (NucliSENS easyQ HPV v1) and dual cytology staining of p16/Ki 67 antibodies (CINtecPLUS). Performance of each biomarker was compared with liquid-based anal cytology. The hypothetical referral rates were defined as the proportion of men who had abnormal cytology or tested positive to each of the biomarkers.

Results: The median age of the 617 participants was 49 years (range: 35-79), and 35.7% were HIV-positive. All biomarkers were strongly associated with the grade of HPV-associated anal lesions (P<0.001 for all). High-risk HPV (HR-HPV) viral load with a 33% cut-off and HR-HPV E6/E7 mRNA had similar sensitivity to anal cytology (78.4 and 75.4 vs. 83.2%, respectively), improved specificity (68.0 and 69.4 vs. 52.4%, respectively) and lower referral rates (47.0 and 45.0 vs. 59.2%, respectively). Specificity was significantly higher in the HIV-negative for HR-HPV viral load (72.3 vs. 58.2%, P=0.005).

Conclusion: HR-HPV viral load and E6/E7 mRNA had similar sensitivity and higher specificity in predicting histological anal high-grade squamous intraepithelial lesion with lower referrals in GBM than anal cytology.

Abstract access

Is a “cure” unrealistic? Long-term remission or maintenance might be the real target for basic scientists

Editor’s notes: News from the Paris IAS conference about the prospects for a cure for HIV was rather sombre this year. Anthony Fauci, Director of NIAID presented a special session in which he suggested that a true “cure” that could be widely used was likely to prove impossible, and that we should think more in terms of long-term remission in the absence of ART. He outlined a vision in which the increasing number of broadly neutralizing antibodies and the discovery of more and more potent antibodies might eventually allow for “maintenance treatment” with subcutaneous antibody injections every few months.

Harper’s commentary lays out some of the amazing steps forward over the past decade in understanding how the reservoir of HIV is formed. We have all heard of CD4 cells, but a much rarer type of lymphocyte, labelled as CD32, seems to be a key target into which HIV integrates. This allows scientists to develop new ways to measure the reservoir and also to begin to determine which cells are involved in establishing and maintaining the reservoir that makes HIV so hard to cure.

Montserrat et al. also provide a sobering result. They showed that as expected the size of the HIV reservoir (as measured by the amount of integrated HIV DNA) falls during long term antiretroviral therapy (ART). When ART is interrupted, HIV begins to replicate and both viral load and the HIV reservoir rebound. Now they have shown that when ART is restarted after the planned interruption,
HIV replication falls promptly, but the HIV reservoir seems to remain high. This may mean that interruption of ART (including in trials of possible long-term remission) may lead to resetting the clock and losing some of the benefits of the long period of HIV treatment prior to the interruption.

HIV reservoirs in children have been less studied than those in adults. So the study by Foster et al. is a useful contribution showing that early ART does lead to a smaller reservoir in children too. This has implications not only for future attempts to “cure” or induce long term remission. It also reduces the pool of variability of the virus in the child, which may make future HIV treatment more straightforward and perhaps reduce the likelihood of developing resistance. It ties in somewhat with another excitement from Paris, which was the report of a child who after early ART had now been in remission with undetectable viral load for more than a decade without taking further ART. There was still evidence of viral DNA, so we cannot talk of cure, but understanding how some children (and adults) are able to control HIV replication after treatment provides an important avenue to explore. Nonetheless, it is crucial to remember that these cases remain very rare, and we should be careful not to encourage false hopes that might lead to people stopping their ART. This should only be done in the context of a very carefully controlled clinical trial situation where close monitoring is available to restart treatment as soon as the virus rebounds.

Impact of long-term antiretroviral therapy interruption and resumption on viral reservoir in HIV-1 infected patients.


We assessed if the increase on viral reservoir after long-term antiretroviral therapy (ART) interruption (ATI) is reversible upon ART resumption in chronic HIV-1 infected patients. Total HIV-1 DNA increased to pre-ART levels after 48 weeks of ATI to return to pre-ATI levels after 104 weeks of ART resumption. Conversely, integrated HIV-1 DNA remained elevated after ART reinitiation. These data suggest that the increase in reservoir after long-term ART discontinuation might not be reversible at mid-term.

Abstract access

Early antiretroviral therapy reduces HIV DNA following perinatal HIV infection.


The impact of antiretroviral therapy (ART) on the size of the HIV reservoir has implications for virological remission in adults, but is not well characterised in perinatally acquired infection (PaHIV). In a prospective observational study of 20 children with PaHIV and sustained viral suppression on ART for >5 years, proviral DNA was significantly higher in deferred (>4 years) versus early (first year of life) ART recipients (p=0.0062), and correlated with age of initiation (p=0.13; r=0.57). No difference was seen in cell-associated viral RNA (p=0.36). Identifying paediatric populations with smaller reservoirs may inform strategies with potential to induce ART-free remission.

Abstract access
**HIV drug resistance – a manageable risk or the harbinger of a “massive second global wave”?**

**Editor’s notes:** The Paris conference also saw the launch of the WHO report and action plan on HIV drug resistance. Laurie Garret writing in Business Insider invoked drug resistance as one of the elements that could lead to a devastating reversal in progress against HIV. Inevitably with increasing scale up of ART, drug resistance levels will begin to rise. In the absence of robust laboratory systems to detect virological failure, the risk is that drug resistance will continue to rise and could threaten progress in some countries. Detection and accurate diagnosis of drug resistance is routine in well-resourced health systems, but still needs to be developed in many of the countries most affected.

While switching to a standard second line regimen provides a public health approach, there will be increasing need for tailored treatment and this requires both strong laboratory systems for sequencing relevant genes, but also good bioinformatic approaches to predict the optimum treatment regimen. Svard et al. used a split genotyping procedure to explore resistance in people failing HIV treatment in Tanzania. This term is used to describe a procedure where the nucleic acid amplification, which requires less sophisticated laboratory systems, is performed locally. The amplified product was then sent to Sweden, where the sequencing and bioinformatics was performed. Tanzania does not yet have widespread access to viral load testing, so treatment failure is defined using the WHO clinical and immunological criteria. In this study, it became clear that as many as two thirds of people thought to be failing treatment were probably not failing virologically, and so were at risk of being changed onto second (or third) line treatments unnecessarily. So the priority should clearly be to establish viral load assays to use to detect treatment failure and to make appropriate switches in treatment. For the minority where failure was truly associated with a raised viral load, resistance mutations showed that people with failure on first line treatment often had viruses that were also resistant to second generation NNRTIs. Current standard second line treatment in Tanzania is with a PI based regimen. Among the first line failure cases, the probability predicted by the bioinformatics for successful second line treatment was around 85% using the medicines registered in Tanzania, which would improve to 95% if all current medicines were available. For people with second-line failure, the corresponding proportions were 79% and 94% respectively.

Inzaule et al. also reported on drug resistance in East Africa. They too showed that one in four patients failing second line treatment across Kenya could not be treated effectively with the medicines currently registered in Kenya.

While drug resistance is certainly a threat to the success of ART programmes, it is important to remember that resistance can be minimised by paying close attention to supporting those on treatment to maximize adherence. Viral load assays need to be cheaper, simpler and more widely available to prevent unnecessary switching. The results of the recent population-based HIV impact assessments (PHIA) are somewhat reassuring. In random population-based surveys in Zimbabwe, Zambia and Malawi, 87%-91% of people taking ART had a suppressed viral load. And in these three countries, the large majority of people are still taking first line treatment and viral load assays are not routinely available. “Alert but not alarmed” was the message from the WHO press release accompanying their report.

**Drug resistance testing through remote genotyping and predicted treatment options in human immunodeficiency virus type 1 infected Tanzanian subjects failing first or second line antiretroviral therapy.**

Introduction: Antiretroviral therapy (ART) has been successfully introduced in low-middle income countries. However an increasing rate of ART failure with resistant virus is reported. We therefore described the pattern of drug resistance mutations at antiretroviral treatment (ART) failure in a real-life Tanzanian setting using the remote genotyping procedure and thereafter predicted future treatment options using rule-based algorithm and the EuResist bioinformatics predictive engine. According to national guidelines, the default first-line regimen is tenofovir + lamivudine + efavirenz, but variations including nevirapine, stavudine or emtricitabine can be considered. If failure on first-line ART occurs, a combination of two nucleoside reverse transcriptase inhibitors (NRTIs) and boosted lopinavir or atazanavir is recommended.

Materials and methods: Plasma was obtained from subjects with first (n = 174) or second-line (n = 99) treatment failure, as defined by clinical or immunological criteria, as well as from a control group of ART naïve subjects (n = 17) in Dar es Salaam, Tanzania. Amplification of the pol region was performed locally and the amplified DNA fragment was sent to Sweden for sequencing (split genotyping procedure). The therapeutic options after failure were assessed by the genotypic sensitivity score and the EuResist predictive engine. Viral load was quantified in a subset of subjects with second-line failure (n = 52).

Results: The HIV-1 pol region was successfully amplified from 55/174 (32%) and 28/99 (28%) subjects with first- or second-line failure, respectively, and 14/17 (82%) ART-naïve individuals. HIV-1 pol sequence was obtained in 82 of these 97 cases (84.5%). Undetectable or very low (<2.6 log$^{10}$ copies/10-3 L) viral load explained 19 out of 25 (76%) amplification failures in subjects at second-line ART failure. At first and second line failure, extensive accumulation of NRTI (88% and 73%, respectively) and NNRTI (93% and 73%, respectively) DRMs but a limited number of PI DRMs (11% at second line failure) was observed. First line failure subjects displayed a high degree of cross-resistance to second-generation NNRTIs etravirine (ETR; 51% intermediate and 9% resistant) and rilpivirine (RPV; 12% intermediate and 58% resistant), and to abacavir (ABC; 49% resistant) which is reserved for second line therapy in Tanzania. The predicted probability of success with the best salvage regimen at second-line failure decreased from 93.9% to 78.7% when restricting access to the NRTIs, NNRTIs and PIs currently available in Tanzania compared to when including all approved drugs.

Discussion: The split genotyping procedure is a potential tool to analyse drug resistance in Tanzania but the sensitivity should be evaluated further. The lack of viral load monitoring likely results in a high false positive rate of treatment failures, unnecessary therapy switches and massive accumulation of NRTI and NNRTI mutations. The introduction of regular virological monitoring should be prioritized and integrated with drug resistance studies in resource limited settings.

Abstract Full-text [free] access

Emergence of untreatable, multidrug-resistant HIV-1 in patients failing second-line therapy in Kenya.


We performed a countrywide assessment of HIV drug resistance among 123 patients with virological failure on second-line antiretroviral therapy (ART) in Kenya. The percentage of patients harbouring intermediate-to-high-level resistance was 27% for lopinavir-ritonavir, 24% for atazanavir-ritonavir and 7% for darunavir-ritonavir, and 25% had complete loss of activity to all available first and second-line drugs. Overall, one in four patients failing second-line ART
have completely exhausted available antiretrovirals in Kenya, highlighting the need for increased access to third-line drugs.

Abstract access

2. Combination prevention

*Age-disparate sexual partnerships - it’s more complicated than sugar daddies and blessers*

Editor’s notes: Sugar daddies and blessers are men who provide gifts, money or other benefits to much younger women in exchange for sex. These relationships are inevitably complex and are often seen as an important mode of transmission for HIV, particularly in Southern and East Africa. Health education campaigns have raised the issue and aimed to discourage young women from having sex with older men. However, the research on age-disparate relationships has been harder to interpret. Some studies show that having older partners is not necessarily an independent risk factor for HIV acquisition and others demonstrate a clear age difference in some couples where phylogenetics makes transmission seem very likely. Nor do all age-disparate relationships involve sugar daddies or blessers. Many women choose partners who are a few years older than themselves without such clear cut transactional motives.

This month saw Akullian et al. conclude that “age of sexual partner is a major risk factor for HIV acquisition” with frighteningly high rates of HIV incidence of 9.7 per 100 person years occurring among women aged 15-24 years old reporting partnerships with men aged 30-34 years old. Yet the same research group (Harling et al.), in the same geographic community three years ago, concluded that “partner age disparity did not predict HIV acquisition” and cautioned against using resources for public health campaigns to reduce such partnerships. A recent paper (de Oliveira et al.) from another research setting, also in KwaZulu-Natal, used phylogenetics to link isolates that were likely to be transmission pairs. They too found that younger women (aged younger than 25 years) were more likely to have older male partners. On average in the couples linked by phylogenetics the age difference was 8.7 years when the woman was younger than 25 but only 1.1 years when she was older than 25 years.

This month Schaefer et al. also demonstrated that in the Manicaland cohort in Zimbabwe, where incidence is somewhat lower than in KwaZulu-Natal, young women aged 15-24 years in partnerships with older men were likely to become HIV positive. They note that even the introduction of ART has not changed this observed finding, suggesting that the failure to reach men as effectively as we are reaching women, may be a significant reason for ongoing transmission.

The Akullian et al. paper used statistical techniques to smooth the observations from more than 1000 seroconversions observed in more than 25 000 person years of follow-up. Harling et al. followed the cohort of women aged 15-29 years in the study area and observed 458 seroconversions over 5913 woman years of observation. Although age-disparate relationships were common, age disparity was not an independent risk factor for HIV infection. Akullian et al. explain that the real risk is from men aged 30-34 years. Men in this age group are more likely to have recently acquired HIV, as it is the peak age group for incidence in males. They are therefore likely to be particularly infectious with higher viral loads. They are also a group that has a low uptake of HIV testing and linkage to ART.

The rates of ART use and HIV prevalence of older male partners for young women was explored by Evans et al. using data from the South African 2012 National HIV survey. They found that male partners who were considerably older were more likely to be taking ART and so were likely to transmit
Sexual partnership age pairings and risk of HIV acquisition in rural South Africa.


Objective: To quantify the contribution of specific sexual partner age groups to the risk of HIV acquisition in men and women in a hyperendemic region of South Africa.

Design: We conducted a population-based cohort study among women (15-49 years of age) and men (15-55 years of age) between 2004 and 2015 in KwaZulu-Natal, South Africa.

Methods: Generalized additive models were used to estimate smoothed HIV incidence rates across partnership age pairings in men and women. Cox proportional hazards regression was used to estimate the relative risk of HIV acquisition by partner age group.

Results: A total of 882 HIV seroconversions were observed in 15,935 person-years for women, incidence rate=5.5 per 100 person-years [95% confidence interval (CI), 5.2-5.9] and 270 HIV seroconversions were observed in 9,372 person-years for men, incidence rate=2.9 per 100 person-years (95% CI, 2.6-3.2). HIV incidence was highest among 15-24-year-old women reporting partnerships with 30-34-year-old men, incidence rate=9.7 per 100 person-years (95% CI, 7.2-13.1). Risk of HIV acquisition in women was associated with male partners aged 25-29 years (adjusted hazard ratio; aHR=1.44, 95% CI, 1.02-2.04) and 30-34 years (aHR=1.50, 95% CI, 1.08-2.09) relative to male partners aged 35 and above. Risk of HIV acquisition in men was associated with 25-29-year-old (aHR=1.72, 95% CI, 1.02-2.90) and 30-34-year-old women (aHR=2.12, 95% CI, 1.03-4.39) compared to partnerships with women aged 15-19 years.

Conclusion: Age of sexual partner is a major risk factor for HIV acquisition in both men and women, independent of one's own age. Partner age pairings play a critical role in driving the cycle of HIV transmission.

Abstract Full-text [free] access

Partner age-disparity and HIV incidence risk for older women in rural South Africa.

While sexual partner age disparity is frequently considered as a potential risk factor for HIV among young women in Africa, no research has addressed this question among older women. Our aim was thus to determine whether sex partner age disparity was associated with subsequent HIV acquisition in women over 30 years of age. To achieve this aim we conducted a quantitative analysis of a population-based, open cohort of women in rural KwaZulu-Natal, South Africa (n = 1737) using Cox proportional hazards models. As partner age rose, HIV acquisition risk fell significantly: compared to a same-aged partner, a 5-year older partner was associated with a one-third reduction [hazard ratio (HR) 0.63, 95% CI 0.52-0.76] and a 10-year older partner with a one-half reduction (HR 0.48, 95% CI 0.35-0.67) in acquisition risk. This result was neither confounded nor effect-modified by women's age or socio-demographic factors. These findings suggest that existing HIV risk-reduction campaigns warning young women about partnering with older men may be inappropriate for older women. HIV prevention strategies interventions specifically tailored to older women are needed.

Abstract Full-text [free] access


Background: The incidence of HIV infection in young women in Africa is very high. We did a large-scale community-wide phylogenetic study to examine the underlying HIV transmission dynamics and the source and consequences of high rates of HIV infection in young women in South Africa.

Methods: We did a cross-sectional household survey of randomly selected individuals aged 15-49 years in two neighbouring subdistricts (one urban and one rural) with a high burden of HIV infection in KwaZulu-Natal, South Africa. Participants completed structured questionnaires that captured general demographic, socioeconomic, psychosocial, and behavioural data. Peripheral blood samples were obtained for HIV antibody testing. Samples with HIV RNA viral load greater than 1000 copies per mL were selected for genotyping. We constructed a phylogenetic tree to identify clusters of linked infections (defined as two or more sequences with bootstrap or posterior support ≥90% and genetic distance ≤4·5%).

Findings: From June 11, 2014, to June 22, 2015, we enrolled 9812 participants, 3969 of whom tested HIV positive. HIV prevalence (weighted) was 59·8% in 2835 women aged 25-40 years, 40·3% in 1548 men aged 25-40 years, 22·3% in 2224 women younger than 25 years, and 7·6% in 1472 men younger than 25 years. HIV genotyping was done in 1589 individuals with a viral load of more than 1000 copies per mL. In 90 transmission clusters, 123 women were linked to 103 men. Of 60 possible phylogenetically linked pairings with the 43 women younger than 25 years, 18 (30·0%) probable male partners were younger than 25 years, 37 (61·7%) were aged 25-40 years, and five (8·3%) were aged 41-49 years: mean age difference 8·7 years (95% CI 6·8-10·6; p<0·0001). For the 92 possible phylogenetically linked pairings with the 56 women aged 25-40 years, the age difference dropped to 1·1 years (95% CI -0·6 to 2·8; p=0·111). 16 (39·0%) of 41 probable male partners linked to women younger than 25 years were also linked to women aged 25-40 years. Of 79 men (mean age 31·5 years) linked to women younger than 40 years, 62 (78·5%)
were unaware of their HIV-positive status, 76 (96·2%) were not on antiretroviral therapy, and 29 (36·7%) had viral loads of more than 50 000 copies per mL.

Interpretation: Sexual partnering between young women and older men, who might have acquired HIV from women of similar age, is a key feature of the sexual networks driving transmission. Expansion of treatment and combination prevention strategies that include interventions to address age-disparate sexual partnering is crucial to reducing HIV incidence and enabling Africa to reach the goal of ending AIDS as a public health threat.

Abstract access

Age-disparate relationships and HIV incidence in adolescent girls and young women: evidence from Zimbabwe.


Objective: Age-disparate sexual relationships with older men may drive high rates of HIV acquisition in young women in sub-Saharan Africa, but evidence is limited. We investigate the association between age-disparate relationships and HIV incidence in Manicaland, Zimbabwe.


Methods: A total of 3746 young women aged 15-24 years participated in consecutive surveys and were HIV-negative at the beginning of intersurvey periods. Last sexual partner age difference and age-disparate relationships [intergenerational (≥10 years age difference) and intragenerational (5-9 years) versus age-homogeneous (0-4 years)] were tested for associations with HIV incidence in Cox regressions. A proximate determinants framework was used to explore factors possibly explaining variations in the contribution of age-disparate relationships to HIV incidence between populations and over time.

Results: About 126 HIV infections occurred over 8777 person-years (1.43 per 100 person-years; 95% confidence interval=1.17-1.68). Sixty-five percent of women reported partner age differences of at least 5 years. Increasing partner age differences were associated with higher HIV incidence [adjusted hazard ratio (aHR)=1.05 (1.01-1.09)]. Intergenerational relationships tended to increase HIV incidence [aHR=1.78 (0.96-3.29)] but not intragenerational relationships [aHR=0.91 (0.47-1.76)]. Secondary education was associated with reductions in intergenerational relationships [adjusted odds ratio (aOR)=0.49 (0.36-0.68)]. Intergenerational relationships were associated with partners having concurrent relationships [aOR=2.59 (1.81-3.70)], which tended to increase HIV incidence [aHR=1.74 (0.96-3.17)]. Associations between age disparity and HIV incidence did not change over time.

Conclusion: Sexual relationships with older men expose young women to increased risk of HIV acquisition in Manicaland, which did not change over time, even with introduction of antiretroviral therapy.

Abstract Full-text [free] access

HIV prevalence and ART use among men in partnerships with 15-29 year old women in South Africa: HIV risk implications for young women in age-disparate partnerships.

This study assesses whether men's ART use mitigates HIV-risk within age-disparate partnerships. Using data from the 2012 South African National HIV survey, we analyzed differences in HIV prevalence and ART use between men in age-disparate and age-similar partnerships with young women aged 15-29 using multiple logistic regression analyses. Within partnerships involving women 15-24 years old, men in age-disparate partnerships were more likely to be HIV-positive (5-9 year age-gap: aOR 2.8, 95%CI 1.4-5.2; p < 0.01; 10+ year age-gap: aOR 2.2, 95%CI 1.0-4.6; p < 0.05). Men in age-disparate partnerships who were 5-9 years older were significantly more likely to be HIV-positive and ART-naïve (aOR 2.4, 95%CI 1.2-4.8; p < 0.05), while this was not the case for men 10+ years older (aOR 1.5, 95%CI 0.7-3.6; p = 0.32). No evidence was found that 25-29 year old women were at greater HIV-risk in age-disparate partnerships. Our results indicate that young women aged 15-24 have a greater likelihood of exposure to HIV through age-disparate partnerships, but ART use among men 10+ years older could mitigate risk.

Abstract access

3. Key populations

Some key considerations for surveys of key populations

Editor's notes: A key challenge for epidemiological research involving key populations is to find a representative sample. Whereas national surveys such as demographic health surveys (DHS) and PHIA can use the total population to create a sampling frame from which to draw individuals at random, researchers interested in key populations have to use a range of methods, all of which have limitations as well as strengths. Internet and app-based surveys may accrue large numbers, but may have significant biases in terms of who chooses to answer such questionnaires. Venue-based sampling allows data to be collected from people who happen to be at the venue at the same time as the researchers. Respondent driven sampling has become increasingly popular as a method to reach individuals that might otherwise be hard to include in studies. Increasingly sophisticated statistical methods have been developed to adjust estimates, and in particular their precision, according to characteristics of respondents found in the sample.

This month we have three respondent driven studies that highlight different methodological aspects as well as shedding light on key populations in Africa and Asia. Hladik et al. conducted a major survey of female sex workers in Kampala, Uganda. Unfortunately, it has taken some time for this study to be published, as the original questionnaires were completed in 2008/9 and it is plausible that many aspects of sex work have been changing over the past decade. Nonetheless, the authors succeeded in enrolling almost 1000 female sex workers from the capital city using a respondent driven sampling approach. The authors paid close attention to methods that could maximize the validity of the data they collected as well as ensuring that participants were protected. Formative research laid out acceptable incentives to participate, as well as approaches to discuss sensitive or taboo areas and to ensure that all the women understood what was being asked in particular questions. Finger scanners were used to generate unique identification numbers, so that women could be tracked during the study, and these files were subsequently deleted. This approach was widely accepted, as it has been in many programmes offering services that benefit from a linked identifier. However, any approach that creates identifiers for populations that are often discriminated or legislated against needs to be examined critically to ensure that any risks to participants are well understood, particularly for research that is not going to bring any direct benefits to the individual participants. Although the study's findings are not particularly surprising, they remind us that sex
workers in Kampala need to remain a vital part of the HIV response. Not only are they affected by a high prevalence of 33%, rising to 44% among those over 25 years old, but they are also subject to horribly high rates of violence including both rape and beating in up to one third of the women in the one month prior to the interview. The study highlights particular factors that might help identify women in most need of HIV and other services. Women with less education, who rely entirely on sex work for their income and who have never tested for HIV are all more likely to be HIV positive.

In nearby Malawi, Wirtz et al. point out that many respondent driven samples of key populations, such as that from Hladik et al., are only able to collect data from one particular city or region, and that this can lead to misinterpretation if the results are generalized to whole countries. The authors conducted a large study of gay men and men who have sex with men in seven different communities across Malawi. They found considerable heterogeneity leading to an overall estimate that the risk of HIV was approximately twice as high in gay men and men who have sex with men as in the general population of men of the same age. The study managed to enrol a total of almost 2500 men through respondent driven sampling in the different districts. However, this was at the expense of having to collect data over a considerable time period, with the study team moving from district to district. As the authors acknowledge, the risk is that data collected in the most recent time period may not be equivalent to data collected four years previously. The authors did find that the highest rates of HIV among gay men and men who have sex with men were not always where they have been presumed to be. In particular tourist areas and some rural areas had higher rates than some of the cities that are usually the focus of key populations programmes. Once again, the finding that so few gay men and men who have sex with men knew their status and were linked to treatment may not be surprising but is still shocking. Only 1% of men found to be positive reported that they were aware of their status. The authors point out the tension between public health and policy in a country where homosexuality is criminalized. If HIV is to be prevented, this tension will need to be resolved.

The third respondent driven sampling study also highlights heterogeneity. Verdery et al. used additional statistical methods to study the network characteristics of people who use drugs in two cities in the Philippines (Cebu and Mandaue). The “small world” phenomenon explains how in more closed settings everyone knows everyone else, and among people who use drugs, many people form part of overlapping networks of needle sharing that allow for rapid propagation of infection. Developing such methods could allow respondent driven samples to yield greater insights in to the epidemiology of HIV in key populations. However, issues of representation both of the sample interviewed and of the broader geographic population of interest will remain important. Quantitative research is certainly essential to understand the population sizes of key populations, and their prevalence, incidence and risk factors of HIV infection. However, research into policy formation; social science research to understand the larger context of HIV and implementation science to determine how better to offer services that engage individuals in HIV testing and care remain a high priority.

Burden and characteristics of HIV infection among female sex workers in Kampala, Uganda - a respondent-driven sampling survey


Background: Sex workers in Uganda are at significant risk for HIV infection. We characterized the HIV epidemic among Kampala female sex workers (FSW).

Methods: We used respondent-driven sampling to sample FSW aged 15+ years who reported having sold sex to men in the preceding 30 days; collected data through audio-computer
assisted self-interviews, and tested blood, vaginal and rectal swabs for HIV, syphilis, neisseria gonorrhea, chlamydia trachomatis, and trichomonas vaginalis.

Results: A total of 942 FSW were enrolled from June 2008 through April 2009. The overall estimated HIV prevalence was 33% (95% confidence intervals [CI] 30%-37%) and among FSW 25 years or older was 44%. HIV infection is associated with low levels of schooling, having no other work, never having tested for HIV, self-reported genital ulcers or sores, and testing positive for neisseria gonorrhea or any sexually transmitted infections (STI). Two thirds (65%) of commercial sex acts reportedly were protected by condoms; one in five (19%) FSW reported having had anal sex. Gender-based violence was frequent; 34% reported having been raped and 24% reported having been beaten by clients in the preceding 30 days.

Conclusions: One in three FSW in Kampala is HIV-infected, suggesting a severe HIV epidemic in this population. Intensified interventions are warranted to increase condom use, HIV testing, STI screening, as well as antiretroviral treatment and pre-exposure prophylaxis along with measures to overcome gender-based violence.

Abstract  Full-text [free] access

Geographical disparities in HIV prevalence and care among men who have sex with men in Malawi: results from a multisite cross-sectional survey.


Background: Epidemiological assessment of geographical heterogeneity of HIV among men who have sex with men (MSM) is necessary to inform HIV prevention and care strategies in the more generalised HIV epidemics across sub-Saharan Africa, including Malawi. We aimed to measure the HIV prevalence, risks, and access to HIV care among MSM across multiple localities to better inform HIV programming for MSM in Malawi.

Methods: Between Aug 1, 2011, and Sept 13, 2014, we recruited MSM into cross-sectional research via respondent-driven sampling (RDS) in seven districts of Malawi. RDS and site weights were used to estimate national HIV prevalence and engagement in care and in multilevel regression models to identify correlates of prevalent HIV infection. The comparative prevalence ratio of HIV among MSM relative to adult men was calculated by use of direct age-stratification.

Findings: 2453 MSM were enrolled with a population HIV prevalence of 18·2% (95% CI 15·5-21·2), as low as 4·1% (2·2-7·6) in Mzuzu and as high as 24·5% (19·5-30·3) in Mulanje. The comparative HIV prevalence ratio was 2·52 when comparing MSM with the adult male population. Age-stratified HIV prevalence showed early onset of infection with 11·8% (95% CI 7·3-18·4) of MSM aged 18-19 years HIV infected. Factors positively associated with HIV infection included being aged 21-30 years and reporting female or transgender identity. Among HIV infected MSM, less than 1% reported ever being diagnosed with HIV infection (0·9%, 95% CI 0·4-2·5) and initiated antiretroviral treatment (0·2%, 0·2-0·3).

Interpretation: HIV disproportionately affects MSM in Malawi with disparities sustained across the HIV care continuum. These issues are geographically heterogeneous and begin among young MSM, supporting geographically focused and age-specific approaches to confidential HIV testing with linkage to HIV services.
Social network clustering and the spread of HIV/AIDS among persons who inject drugs in two cities in the Philippines


Introduction: The Philippines has seen rapid increases in HIV prevalence among people who inject drugs. We study two neighboring cities where a linked HIV epidemic differed in timing of onset and levels of prevalence. In Cebu, prevalence rose rapidly from under 1% to 54% between 2009 and 2011 and remained high through 2013. In nearby Mandaue, HIV remained below 4% through 2011 then rose rapidly to 38% by 2013.

Objectives: We hypothesize that infection prevalence differences in these cities may owe to aspects of social network structure, specifically levels of network clustering. Building on prior research, we hypothesize that higher levels of network clustering are associated with greater epidemic potential.

Methods: Data were collected with respondent-driven sampling among males who inject drugs in Cebu and Mandaue in 2013. We first examine sample composition using estimators for population means. We then apply new estimators of network clustering in respondent-driven sampling data to examine associations with HIV prevalence.

Results: Samples in both cities were comparable in terms of composition by age, education, and injection locations. Dyadic needle sharing levels were also similar between the two cities, but network clustering in the needle sharing network differed dramatically. We found higher clustering in Cebu than Mandaue, consistent with expectations that higher clustering is associated with faster epidemic spread.

Conclusion: This paper is the first to apply estimators of network clustering to empirical respondent-driven samples, and it offers suggestive evidence that researchers should pay greater attention to network structure’s role in HIV transmission dynamics.