Welcome to the 5th issue of 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

Do people take more risks when they know they are “protected”? 

Editor’s notes: Risk compensation is a phenomenon well known to behavioural scientists. When car-drivers wear seat belts, they may drive faster because they feel safer. Despite some evidence to the contrary, a commonly voiced concern about PrEP is that people who take it will take more risks with their sexual health. So it is reassuring to see two studies that examine partnership dynamics and condom use among people on antiretroviral therapy (ART) and among men who have been circumcised.

McGrath and Grapsa studied relationships and reported sexual behaviour among 632 people living with HIV and enrolled in an ongoing cohort study in KwaZulu Natal during the period, when only those with lower CD4 counts were eligible for ART. They interviewed participants every 6 months, in person or by phone, for up to 36 months. This was in order to follow which relationships were formed and which dissolved and to determine how often participants were having sex and how often they were having condomless sex. The authors clearly document (perhaps unsurprisingly) that many relationships dissolved (192 out of 565 partnerships at some time in the study) or formed (161 out of 132 individuals who were single at some time in the study). Partnerships dissolved more frequently among people who had only been in a relationship for less than a year; people who drank alcohol and in partnerships where the participant described the relationship as being of “poor quality”. New partners were more common for people who were younger; had not disclosed their HIV status; drank alcohol or reported having more than 3 lifetime sexual partners at the start of the study. There was no suggestion that being on ART affected the likelihood of forming or leaving a partnership. This is important for mathematical models of HIV transmission in the era of universal treatment policies.

Sex was more frequently reported in people in more recent partnerships; people who knew their partners’ HIV status and among people who wanted more children. Sex was less frequent and more often protected by a condom among people who did not trust their partner’s fidelity or where the couple did not live together. People who were eligible for ART tended to use condoms more regularly during the follow up than people who were still “waiting for treatment”. Other factors associated with more condom use included more equitable gender norms; HIV status disclosure and not living together. Condoms were used less often in partnerships that included alcohol, partner violence or where the couple wanted more children. Overall, the authors estimated that around 5.5% of sex acts were “risky” (that is unprotected with a partner who was HIV negative or where the HIV status was unknown) among those eligible for ART and around 13.2% for those not yet eligible. Around one third of the participants reported having condomless sex at least once, but in almost half of these, they knew that their partner was also living with HIV.

Taking effective ART regularly means that people living with HIV are no longer infectious once their viral load is reliably suppressed. However, it is clear that not everyone achieves viral load suppression. This study provides useful prospective information about partnerships and sexual behaviour in the context of very high HIV transmission. It is reassuring in showing that on the whole, sexual behaviour seems less risky, even before taking the huge effect of ART into account. There was no evidence to suggest that risk compensation occurred in those offered ART.

In order to maximize the preventive benefits of ART, it is essential that people are supported to take their medicines regularly. In crowded urban facilities in high prevalence settings, long waiting times, and challenges in stock management mean that people living with HIV have to be quite determined to negotiate the systems and minimize treatment interruptions. Although it is national policy in Zambia and some other highly burden countries to provide three-month supplies to people whose HIV is
stable and well controlled, McCarthy and colleagues found that less than half of people who should be getting three-month refills were doing so. They instituted a cluster randomized trial of a quality improvement programme across 16 health facilities in Lusaka. Each clinic follows around 4-5000 people on ART of whom around 1000 are stable and eligible for three-monthly refills. The key element was for a focal point in each of the eight intervention clinics to be designated as a quality improvement officer and to be supported with materials to plan and monitor drug stocks and support local changes. This is to ensure that stable patients did not have to spend long periods in the clinic or go away with less medicine than they needed. The District Health Management team supported the quality improvement officers when the challenges identified were beyond their responsibilities or capabilities to change. The programme led to a statistically significant 15% increase in the proportion of appropriate people receiving three-month refills (reaching 69%). On average the intervention clinics became less congested (35 fewer visits per day compared to the controls) and had shorter waiting times (20 minutes shorter per visit) although these results did not reach statistical significance.

Another study exploring risk compensation was carried out by Shi and colleagues. The authors used data from recent demographic and health surveys from countries that are part of the scale-up of voluntary medical male circumcision in East and Southern Africa. Circumcision was most prevalent in Kenya (88% and 94% before and after 2008, when scale-up was pushed) and lowest in Zimbabwe (12% and 11% respectively). Overall condom usage increased in both circumcised and uncircumcised men. Reports of condom use at last sex averaged around 15-16% before 2008 across the ten countries surveyed and rose to around 21% after 2008. There was no suggestion that men who were circumcised were any less likely to use a condom than men who were not. Similarly, there was no suggestion that circumcised men were more likely to have non-cohabiting partners.

The study also highlights big differences between countries, and between different groups. Even among men with no regular partner, the use of a condom at last sex is often less than 50% with differences as expected also seen by age, education, religion and residence. Promoting circumcision remains a hugely cost-effective approach to HIV prevention. This study therefore provides important reassurance that the possibility of risk compensation is not serious for circumcision programmes. Nonetheless we still have plenty of work to do to reach our targets and prevent HIV.

Does ART change partnership dynamics and HIV risk behaviours among PLWH? A cohort study in KwaZulu-Natal, South Africa.

McGrath N, Grapsa E. AIDS. 2017 Apr 10. doi: 10.1097/QAD.0000000000001502. [Epub ahead of print]

Objective: We explore the impact of antiretroviral therapy (ART) on partnership acquisition and dissolution rates and changes in sexual behaviours among HIV-infected adults.

Design: Using detailed longitudinal data from a prospective cohort of HIV-infected adults with CD4<200 cell/ml (ART-eligible) or CD4>500 cell/ml (pre-ART) conducted in rural KwaZulu-Natal, South Africa, 2009-2012.

Methods: Partnership acquisition and dissolution are explored through survival analysis methods, while generalized linear models were fitted for the sexual behaviour outcomes with interaction terms to allow the association with ART to vary over time. Throughout, the primary comparison of interest for each outcome is differences between the two ART groups.

Results: ART is not associated with partner acquisition or relationship dissolution. During follow-up, the two ART groups do not differ in the odds of being sexually active nor the number of sex acts, while the odds of unprotected sex are significantly lower for partnerships of ART-eligible
participants, aOR = 0.26, 95% CI (0.15, 0.43). Relationship-level characteristics including cohabitation status and wanting more children with that partner are associated with higher odds and increased frequency of sexual activity, increased odds of unprotected sex; while living with partner, higher relationship quality and longer relationship duration are associated with lower risk of partnership dissolution.

Conclusion: Being on ART was not associated with increased sexual risk behaviours, a reassuring finding given the WHO recommends ART initiation upon HIV diagnosis. The importance of relationship-level characteristics provides evidence that HIV care services should offer routine support for HIV disclosure and sexual risk reduction, and promotion of couples-testing and positive couple-relationships.

Abstract access

Quality improvement intervention to increase adherence to ART prescription policy at HIV treatment clinics in Lusaka, Zambia: A cluster randomized trial.


Introduction: In urban areas, crowded HIV treatment facilities with long patient wait times can deter patients from attending their clinical appointments and picking up their medications, ultimately disrupting patient care and compromising patient retention and adherence.

Methods: Formative research at eight facilities in Lusaka revealed that only 46% of stable HIV treatment patients were receiving a three-month refill supply of antiretroviral drugs, despite it being national policy for stable adult patients. We designed a quality improvement intervention to improve the operationalization of this policy. We conducted a cluster-randomized controlled trial in sixteen facilities in Lusaka with the primary objective of examining the intervention’s impact on the proportion of stable patients receiving three-month refills. The secondary objective was examining whether the quality improvement intervention reduced facility congestion measured through two proxy indicators: daily volume of clinic visits and average clinic wait times for services.

Results: The mean change in the proportion of three-month refills among control facilities from baseline to endline was 10% (from 38% to 48%), compared to a 25% mean change (an increase from 44% to 69%) among intervention facilities. This represents a significant 15% mean difference (95% CI: 2%-29%; P = 0.03) in the change in proportion of patients receiving three-month refills. On average, control facilities had 15 more visits per day in the endline than in the baseline, while intervention facilities had 20 fewer visits per day in endline than in baseline, a mean difference of 35 fewer visits per day (P = 0.1). The change in the mean facility total wait time for intervention facilities dropped 19 minutes between baseline and endline when compared to control facilities (95% CI: -10.2 to -48.5; P = 0.2).

Conclusion: A more patient-centred service delivery schedule of three-month prescription refills for stable patients is viable. We encourage the expansion of this sustainable intervention in Zambia’s urban clinics.

Abstract Full-text [free] access
Evidence that promotion of male circumcision did not lead to sexual risk compensation in prioritized sub-Saharan countries.


Background: WHO and UNAIDS prioritized 14 eastern and southern African countries with high HIV and low male circumcision prevalence for a voluntary medical male circumcision (VMMC) scale-up in 2007. Because circumcision provides only partial protection against HIV infection to men, the issue of possible risk compensation in response to VMMC campaigns is of particular concern. In this study, we looked at population-level survey data from the countries prioritized by WHO for a VMMC scale-up. We compared the difference in sexual risk behaviours (SRB) between circumcised and uncircumcised men before and after the WHO's official VMMC promotion.

Materials and Methods: Ten countries (Kenya, Lesotho, Malawi, Mozambique, Namibia, Rwanda, Tanzania, Uganda, Zambia and Zimbabwe) participating in the WHO's VMMC scale-up had available data from the Demographic and Health Surveys (DHS). We used cumulative-link mixed models to investigate interactions between survey period and circumcision status in predicting SRB, in order to evaluate whether the difference between the behavior of the two groups changed before and after the scale-up, while controlling for socio-demographic and knowledge-related covariates. The main responses were condom use at last sex and number of non-cohabiting sexual partners, both in the last 12 months.

Results: There was little change in condom use by circumcised men relative to uncircumcised men from before the VMMC scale up to after the scale up. The relative odds ratio is 1.06 (95% CI, 0.95-1.18; interaction P = 0.310). Similarly, there was little change in the number of non-cohabiting partners in circumcised men (relative to uncircumcised men): the relative odds ratio of increasing the number of partners is 0.95 (95% CI, 0.86-1.05; interaction P = 0.319). Age, religion, education, job, marital status, media use and HIV knowledge also showed statistically significant association with the studied risk behaviours. We also found significant differences among countries, while controlling for covariates.

Conclusions: Overall, we find no evidence of sexual risk compensation in response to VMMC campaigns in countries prioritized by WHO. Changes in relative partner behaviour and the relative odds of condom use were small (and of uncertain sign). In fact, our estimates, though not significant, both suggest slightly less risky behavior. We conclude that sexual risk compensation in response to VMMC campaigns has not been a serious problem to date, but urge continued attention to local context, and to promulgating accurate messages about circumcision within and beyond the VMMC context.

Abstract Full-text [free] access

Do people living with HIV live well with HIV in the era of antiretroviral therapy?

Editor’s notes: As treatment for HIV becomes increasingly widespread, and HIV-related deaths continue to decline, more and more attention is being paid to chronic non-communicable diseases and to the overall quality of life of people living with HIV. However, despite 71% of people living with HIV in sub-Saharan Africa there is little research on the impact of illness and treatment on quality of life in the region.
Nyongesa and colleagues provide a fascinating mixed methods study, nested within a larger study of children and adolescents with HIV, which begins to formulate and validate a culturally appropriate tool to measure quality of life in the Swahili speaking population of coastal Kenya. They used the functional assessment of HIV infection (FAHI) questionnaire as the starting point. This is an HIV specific adaptation of a tool initially used among people with cancer and widely validated and studied in European and US based populations. 47 questions are used to assess HIV-specific quality of life in five domains: physical; emotional; functional and global well being; social; and cognitive functioning.

Following a scoping literature review, the authors used qualitative interviews with 38 participants living with HIV (largely female [27]) to explore their perceptions of the impact of HIV in the day-to-day life of people living with HIV in general. The issues raised overlapped with all the domains of FAHI except cognitive functioning, which the authors suggest is perhaps under-recognized when there are many competing stressors on people’s lives. The participants then answered a draft version of the FAHI, which had been translated, back translated and reviewed in a group to ensure comprehension and relevance. Following adaptation, the FAHI Swahili version was then administered to a sample of 103 randomly selected study participants living with HIV and on antiretroviral therapy from the same study site. The sample was almost entirely female (94%) reflecting their availability at the parent study centre, which focussed on children and adolescents living with HIV. Overall, the authors conclude that the new adaptation of the tool seems appropriate for further research studies on quality of life among people living with HIV on treatment in East Africa. While the study provides a great example of a serious approach to develop, standardize and validate a culturally appropriate tool, the qualitative results also provide considerable insight into the many ways in which HIV affects these Kenyan’s lives beyond the purely medical. Well worth reading the open access paper.

A study in Europe focussed specifically on the health-related domain of quality of life in Amsterdam. Langebeek and colleagues used two tools that are well validated in European settings to assess physical and mental health related quality of life in 541 individuals living with HIV and 526 control participants without HIV. HIV infection was clearly associated with worse quality of life, both mental and physical despite most participants being well controlled on ART. As we might expect, people who had multiple co-morbidities were less likely to have a good quality of life regardless of HIV status, but HIV remained an independent predictor of poor quality of life. For mental health, HIV and younger age were both independently associated with less good quality of life. The clear message is that we need to look beyond antiretroviral therapy and provide good holistic care including both mental and physical health services for people living with HIV, particularly as the population gets older.

A related study from Gonciulea and colleagues shows that among older men living with HIV, there is a significant increase in the risk of osteoporosis related fractures. Bone demineralization is known to occur with risk factors such as age, sex, and low body mass index (BMI). However, increasingly studies are showing that HIV-related factors, such as antiretroviral medicines, ongoing viral replication and ongoing inflammation, are also potential risk factors. The authors used the multicenter AIDS cohort study to compare fracture incidence rates among 1221 men living with HIV and 1408 HIV-negative men. Both cohorts were aged over 40 years. As expected, fractures occurred more commonly as people got older, but the people living with HIV developed more fractures at an earlier age. This study therefore reinforces the previous one, with the possibility to offer osteoporosis screening to men over the age of 50 who are living with HIV.

Petraglia and colleagues also explored the challenge of osteoporosis in people living with HIV. Chronic obstructive pulmonary disease is known to be associated with low bone mineral density (BMD) and greater fracture risk in HIV negative smokers. In fact the finding of emphysema alone on CT imaging is a strong, independent predictor of osteoporosis in this group. We are beginning to
observe obstructive lung disease as a common comorbidity in people living with HIV and emphysema has been shown to occur at an earlier age with less tobacco exposure in HIV positive smokers. The authors therefore aimed to determine whether CT scans alone could predict who would turn out to have osteoporosis among people living with HIV. As expected, they found that, among 164 people living with HIV, age; smoking and emphysema on CT scan were all associated with reduced BMD in the thoracic spine (estimated from the CT scan). However, they also found that the emphysematous changes were an independent marker for this measure of osteoporosis regardless of age, sex, smoking, and use of antiretroviral medicines or steroids. If a CT scan or lung function test suggests obstructive airways disease or emphysema, we should have a higher index of suspicion for osteoporosis among people living with HIV.

A mixed methods approach to adapting and evaluating the functional assessment of HIV infection (FAHI), Swahili version, for use with low literacy populations.


Background: Despite bearing the largest HIV-related burden, little is known of the Health-Related Quality of Life (HRQoL) among people living with HIV in sub-Saharan Africa. One of the factors contributing to this gap in knowledge is the lack of culturally adapted and validated measures of HRQoL that are relevant for this setting.

Aims: We set out to adapt the Functional Assessment of HIV Infection (FAHI) Questionnaire, an HIV-specific measure of HRQoL, and evaluate its internal consistency and validity.

Methods: The three phase mixed-methods study took place in a rural setting at the Kenyan Coast. Phase one involved a scoping review to describe the evidence base of the reliability and validity of FAHI as well as the geographical contexts in which it has been administered. Phase two involved in-depth interviews (n = 38) to explore the content validity, and initial piloting for face validation of the adapted FAHI. Phase three was quantitative (n = 103) and evaluated the internal consistency, convergent and construct validities of the adapted interviewer-administered questionnaire.

Results: In the first phase of the study, we identified 16 studies that have used the FAHI. Most (82%) were conducted in North America. Only seven (44%) of the reviewed studies reported on the psychometric properties of the FAHI. In the second phase, most of the participants (37 out of 38) reported satisfaction with word clarity and content coverage whereas 34 (89%) reported satisfaction with relevance of the items, confirming the face validity of the adapted questionnaire during initial piloting. Our participants indicated that HIV impacted on their physical, functional, emotional, and social wellbeing. Their responses overlapped with items in four of the five subscales of the FAHI Questionnaire establishing its content validity. In the third phase, the internal consistency of the scale was found to be satisfactory with subscale Cronbach's α ranging from 0.55 to 0.78. The construct and convergent validity of the tool were supported by acceptable factor loadings for most of the items on the respective sub-scales and confirmation of expected significant correlations of the FAHI subscale scores with scores of a measure of common mental disorders.

Conclusion: The adapted interviewer-administered Swahili version of FAHI questionnaire showed initial strong evidence of good psychometric properties with satisfactory internal consistency and acceptable validity (content, face, and convergent validity). It gives impetus for further validation work, especially construct validity, in similar settings before it can be used for research and clinical purposes in the entire East African region.

Abstract Full-text [free] access
Impact of co-morbidity and aging on health-related quality of life in HIV-positive and HIV-negative individuals.


Background: HIV-infected individuals may be at risk for the premature onset of age-associated non-communicable comorbidities. Being HIV-positive, having comorbidities and being of higher age may adversely impact health-related quality of life (HRQL). We investigated the possible contribution of HIV infection, comorbidities, and age on HRQL and depression.

Methods: HIV-infected individuals and uninfected controls from the AGEhIV Cohort Study were screened for the presence of co-morbidities. They completed the Short Form 36-item Health Survey to assess HRQL and the nine-item Patient Health Questionnaire to assess depression. Linear and logistic regression were used to investigate to which extent co-morbidities, aging and HIV infection were independently associated with HRQL and depression.

Results: HIV-infected individuals (n=541) reported significantly worse physical and mental HRQL and had a higher prevalence of depression than HIV-uninfected individuals (n=526). A higher number of co-morbidities and HIV-positive status were each independently associated with worse physical HRQL, whereas HIV-positive status and younger age were independently associated with worse mental HRQL and more depression. The difference in physical HRQL between HIV-positive and HIV-negative individuals did not become greater with a higher number of co-morbidities or with higher age.

Conclusions: In a cohort of largely well-suppressed HIV-positive participants and HIV-negative controls, HIV-positive status was significantly and independently associated with worse physical and mental HRQL and with an increased likelihood of depression. Our finding that a higher number of co-morbidities was independently associated with worse physical HRQL reinforces the importance to optimize prevention and management of co-morbidities as the HIV-infected population continues to age.

Abstract access

An increased rate of fracture occurs a decade earlier in HIV+ compared to HIV- men in the Multicenter AIDS Cohort Study (MACS).


Objectives: To determine the incidence and age-related fracture risk among HIV-infected (HIV+) and uninfected men (HIV-). To evaluate factors independently associated with fracture risk.

Design: Prospective, multicenter cohort study of men with or at risk for HIV.

Methods: Outcome measures: 1) all fractures (excluding skull, face, digits) and 2) fragility fractures (vertebral column, femur, wrist, humerus) were collected semiannually in 1221 HIV+ and 1408 HIV-men ≥ age 40. Adjusted incident rate ratios (aIRR) with an interaction term for age (40-49, 50-59, ≥60 years) and HIV serostatus were estimated with Poisson regression models accounting for additional risk factors.
Results: Fracture incidence increased with age among both HIV+ and HIV- men. While there was no significant difference in fracture incidence by HIV serostatus among men aged 40-49 years, the HIV+ men aged 50-59 years had a significantly higher incidence of all fractures (aIRR = 2.06 [1.49, 2.84]) and fragility fractures (aIRR = 2.06 [1.21, 3.50]) compared with HIV- participants of similar age. HIV modified the effect of age on all fractures (p = 0.002) but did not significantly modify the effect for fragility fractures (p = 0.135). Hypertension increased the rate of all fractures by 32% after adjustment for covariates (aIRR = 1.32 [1.04, 1.69]).

Conclusions: Fracture incidence increased with age among HIV+ and HIV- men but was higher among HIV+ men. A significant increase in fracture incidence was found among 50-59-year-old HIV+ men, highlighting the importance of osteoporosis screening for HIV infected men above the age of 50.

Abstract access

Emphysema is associated with thoracic vertebral bone attenuation on chest CT scan in HIV-infected individuals.


Background: Age-related chronic diseases are prevalent in HIV-infected persons in the antiretroviral therapy (ART) era. Bone mineral density (BMD) loss and emphysema have separately been shown to occur at a younger age and with lesser risk exposure in HIV-infected compared to HIV-uninfected individuals. In non-HIV infected smokers, emphysema has been shown to independently predict low BMD. We hypothesized that emphysema would independently associate with thoracic vertebral bone attenuation, a surrogate for bone mineral density, in HIV-infected individuals.

Methods: Clinical, pulmonary function, and radiographic data were analyzed for 164 individuals from the University of Pittsburgh’s HIV Lung Research Center cohort. Chest CT scans were used to quantify emphysema and compute Hounsfield Unit (HU) attenuation of the 4th, 7th, and 10th thoracic vertebrae. The association between mean HU attenuation values across the three vertebrae and radiographic emphysema, age, sex, body mass index (BMI), steroid use, viral load, CD4 count, and forced expiratory volume in the first second (FEV1) was assessed by univariate and multivariate analyses.

Results: In univariate analysis, mean HU attenuation decreased with increasing age (p<0.001), pack years (p = 0.047), and percent emphysema (p<0.001). In a multivariable model, including pack years, age, sex, ART and steroid use, greater emphysema was independently associated with this surrogate marker of BMD in HIV-infected individuals (p = 0.034).

Conclusions: The association of emphysema with thoracic bone attenuation in HIV-infected individuals is consistent with previous reports in non-HIV infected smokers. These findings suggest that emphysema should be considered a potential marker of osteoporosis risk in HIV-infected individuals.

Abstract Full-text [free] access

2. Elimination of childhood infections
Increasing HIV testing by sharing the load and updating tasks and traditions for traditional birth attendants and lay providers.

Editor’s notes: Nigeria still has the highest number of new HIV infections among children in the world, around 40,000 annually, with the large majority arising from mother to child transmission. In Nigeria, less than 20% of pregnant women receive HIV testing. This is due to several issues which include a limited number of HIV testing service delivery points and a limited number of deliveries taking place at health facilities. Around two thirds of deliveries take place at home, traditionally supported by traditional birth attendants (TBAs). Many TBAs in Nigeria have little knowledge of either the benefits or practice of HIV testing, nor of ways to reduce transmission of HIV to infants.

Chizoba and colleagues have developed and tested a model of antenatal care that aims to integrate TBAs within the government primary health care (PHC) network. The intervention consisted of PHC clinics identifying a few TBAs who operated in the catchment area of the clinic. Between one and five of these TBAs was invited to the PHC clinic for a one-day training on HIV point of care testing, and asked to refer all women found to be positive to the clinic for confirmation and follow up. Once a month TBAs came to the clinic for encouragement and to provide data on tests performed. Once a quarter, the clinic visited the TBAs to provide supervision, mentoring and quality improvement training. The TBAs were also paid $2 for every pregnant woman whom they tested for HIV, in order to compensate them for any loss of earnings from pregnant women living with HIV who would now be seen in the clinic rather than delivering at home.

The authors used a quasi-experimental design for this study. Out of the 74 PEPFAR supported PHC clinics that provided HIV services in their antenatal clinics in Ebonyi state of Nigeria, 34 were interested in this new integrated approach, whereas 40 expressed no interest. 20 clinics were chosen at random from each of these categories, to avoid additional selection bias. (Although as the authors state, there may already be considerable differences between the clinics that were interested and clinics that were not). Comparisons were made before and after the programme was put in place, and also between clinics in the intervention group and those in the group that had not been interested to integrate services with the TBAs.

Despite this non-randomized design, the results are quite striking with more than twice as many women receiving HIV testing in the intervention clinics in the six months after the intervention began (going up from 2501 to 5346 across the 20 clinics). There was no such increase in the non-intervention areas (which saw a change from 1770 to 1892 across the 20 clinics). Furthermore the large majority of the increase was among women who had been tested by the TBAs.

While this is hugely encouraging and a big increase, it will be important to see if the increase can be sustained as it is a significant change in the way that the TBAs and the PHC clinic staff work. It is also not clear how much the increase is a result of the integration model and how much it relates to the additional payment that TBAs receive, which seems to amount to around $100 per TBA over the 6 month period of the assessment.

A thorough review of the role of trained lay providers in performing HIV tests was carried out as part of the WHO process that led to the guidance in 2015 that “Lay providers who are trained and supervised to use rapid diagnostic tests (RDTs) can independently conduct safe and effective HIV testing services.” Kennedy and colleagues now present the details of that systematic review.

Many national policies, particularly in African countries allow for HIV testing by trained lay providers using rapid diagnostic tests (RDTs) and even more allow lay providers to perform pre- and post-test counselling (around 80% of African countries in one survey of policies). However, some countries limit these roles to trained healthcare providers due to concerns about lay providers’ ability to perform
the tests accurately and reliably and to deliver high quality pre- and post-test counselling, linkage to appropriate prevention and clinical care services, and coordination with laboratory services to ensure the delivery of correct test results.

Despite widespread use of lay providers, there are actually rather few studies that directly compare the outcomes of testing between lay and professional providers. The authors reviewed over 6000 titles, abstracts or full articles and found only five that allowed a direct comparison, while an additional six studies allowed the values and preferences of clients and providers to be assessed.

While this evidence base is very limited, findings from the single randomized trial (in the US) and one observational study (in Malawi), that compared pre- and post-intervention time periods, suggest that using trained lay providers can increase HIV testing uptake. Three studies compared the quality of testing between lay providers and professional providers and found that both can achieve similar testing quality. Unfortunately, no studies measured adverse events following testing, nor linkage to care. The six values and preferences studies, also found support for lay providers.

This is the key evidence that underpins the strong recommendation from WHO and now also from many national authorities, that trained lay providers are an essential component in the efforts to scale up HIV testing in order to reach the first 90.

Increasing HIV testing among pregnant women in Nigeria: evaluating the traditional birth attendant and primary health center integration (TAP-In) model.


Engaging Traditional Birth Attendants (TBAs) may be critical to preventing mother-to-child transmission of HIV (PMTCT) in Nigeria. We integrated TBAs into Primary Health Centers (PHCs) and provided the TBAs with HIV counseling and testing (HCT) training for PMTCT (TAP-In). The purpose of this study was to evaluate the impact of TAP-In on HCT uptake among pregnant women. A quasi-experimental design was used for this study. Twenty PHCs were assigned to the intervention group that integrated TAP-In and 20 were assigned to the control group. Data were collected six months prior to the initiation of TAP-In and six months post, using antenatal clinic registries. Intervention PHCs more than doubled the number of pregnant women who received HCT in their catchment area post TAP-In while control PHCs had no significant change. After initiating TAP-In, intervention PHCs provided almost three times more HCT than the control PHCs (p < 0.01) with TBA provided over half of the HCT post TAP-In. The TAP-In model was effective for increasing HCT among pregnant women.

Abstract access

Should trained lay providers perform HIV testing? A systematic review to inform World Health Organization guidelines.


New strategies for HIV testing services (HTS) are needed to achieve UN 90-90-90 targets, including diagnosis of 90% of people living with HIV. Task-sharing HTS to trained lay providers may alleviate health worker shortages and better reach target groups. We conducted a systematic review of studies evaluating HTS by lay providers using rapid diagnostic tests (RDTs). Peer-reviewed articles were included if they compared HTS using RDTs performed by trained lay providers to HTS
by health professionals, or to no intervention. We also reviewed data on end-users' values and preferences around lay providers performing HTS. **Searching was conducted through 10 online databases, reviewing reference lists, and contacting experts.** Screening and data abstraction were conducted in duplicate using systematic methods. Of 6113 unique citations identified, 5 studies were included in the effectiveness review and 6 in the values and preferences review. One US-based randomized trial found patients' uptake of HTS doubled with lay providers (57% vs. 27%, percent difference: 30, 95% confidence interval: 27-32, p < 0.001). In Malawi, a pre/post study showed increases in HTS sites and tests after delegation to lay providers. Studies from Cambodia, Malawi, and South Africa comparing testing quality between lay providers and laboratory staff found little discordance and high sensitivity and specificity (≥98%). Values and preferences studies generally found support for lay providers conducting HTS, particularly in non-hypothetical scenarios. Based on evidence supporting using trained lay providers, a **WHO expert panel recommended lay providers be allowed to conduct HTS using HIV RDTs.** Uptake of this recommendation could expand HIV testing to more people globally.

Abstract Full-text [free] access

3. Combination prevention

*How do we know which activities make a difference to HIV prevention?*

**Editor's notes:** In order to be fairly certain that an intervention is responsible for changes in HIV or HIV-related behaviours, the gold standard is randomization. This allows for fair comparisons between groups, since factors that might alter the outcomes will be more or less equally balanced between the study groups. This is true whether such confounding factors are expected, but also importantly, even those factors that are unknown, unexpected and unmeasured will also be balanced between the arms.

A second key determinant of high quality research is to use an approach that maximizes full engagement and follow-up of participants in the study. One such approach that is widely recognized is to use Good Participatory Practice.

Rhodes and colleagues study condom promotion and HIV testing among the Hispanic/Latino community of gay men and other men who have sex with men in North Carolina, USA. Although gay men and other men who have sex with men represent approximately 4% of the adult male population in the United States of America, they account for more than 80% of new HIV infections among men. Around one quarter of gay men and other men who have sex with men are Hispanic or Latino. The authors therefore wanted to use research to make a difference to the HIV burden of the Hispanic/Latino gay men and other men who have sex with men community in North Carolina, USA. They found that despite the impact of HIV on Hispanic/ Latino gay men and other men who have sex with men, they were only able to identify one evidence-based behavioural HIV prevention programme focused on this population.

The authors used an extensive community based participatory research partnership, whose members represented the Hispanic/ Latino gay men and other men who have sex with men community, AIDS service organizations, Hispanic/Latino-serving community organizations, and universities to develop, implement, and evaluate a Spanish-language, small group intervention designed to increase condom use and HIV testing among Hispanic/Latino gay men and other men who have sex with men (HOLA en Grupos).
304 participants were randomly allocated to the HOLA en Grupos intervention, or to a general health education comparison intervention having the same number of sessions (4) and duration (16 hours in total) that focussed on prostate, lung, and colorectal cancers; diabetes; high cholesterol; cardiovascular disease; and alcohol misuse. These topics for the control group were identified on the basis of identified needs and priorities of Hispanic/Latino gay men and other men who have sex with men.

HOLA en Grupos is grounded on social cognitive theory, empowerment education, and traditional Hispanic/Latino cultural values and includes four interactive modules of four hours each delivered in groups. Participants in both intervention and control arms received reimbursement for their time, certificates of completion and meals and a celebration at the completion of the course. In other words this was an intensive intervention that might be hard to replicate in most settings, but it follows very high standards both for developing and conducting the research and also for determining the impact of the intervention.

The intervention was associated with a large effect on both condom usage (four-fold higher in the intervention arm than the control) and HIV test uptake (an astonishing 14-fold higher, reflecting the relatively low testing rate in the control group).

A major limitation in many HIV prevention studies, including this one, is that the outcome is based on reported behaviour. The challenge is that the real outcome of interest, which is new HIV infections, is relatively rare in almost all communities so that studies have to be huge and expensive, and the large majority of participants in both intervention and control arms do not in fact acquire HIV. This is in contrast to most studies of treatment, where there are clearly defined biological, standardized measures which many or all participants are likely to reach. Nonetheless, there are many examples of studies that find changes in reported behaviour that are not associated with biological markers of such change (such as incidence of HIV or other sexually transmitted infections, or pregnancy).

There are also many observational or ecological studies that report changes in new HIV infections but that cannot truly say why the number of infections fell and whether the interventions used in the study were responsible for the changes. For example Nwokolo and colleagues report in a short research letter on the dramatic decline in new HIV diagnoses in the large London clinic where they work. New infections in that clinic, and in fact in other large clinics in London, have dropped by a remarkable 40% from 2015 to 2016, as originally reported in the popular science press before any scientific publication or presentation. The authors of the research letter are suitably cautious about how to account for the impressive decline. Various systems have been improved over the past few years in this clinic to make it easier to have an HIV test and start treatment immediately. However, most of the clinic team (and many other commentators) assume that it is also due to the rapid rise in the use of PrEP. Although it is still not available through the UK National Health Service, the clinic has been at the forefront of encouraging gay men and other men who have sex with men who might benefit from PrEP to purchase it from on-line pharmacies. The clinic then provides the appropriate monitoring and follow up to ensure that their clients get the best possible PrEP service given the current constraints. Whatever the cause, we should be celebrating the rapid fall in new HIV infections across London, which is home to a substantial proportion of the new HIV infections in the UK.

The challenges of demonstrating evidence of effectiveness for HIV prevention is also felt among black women in the USA. Although they have the highest burden of HIV among women in the USA, the incidence rates are such that a traditional randomized trial design would need to be huge, and consequently hugely expensive. Adimora and colleagues consider whether an alternative trial design might be to use data from high HIV incidence settings and then to develop proxies of protection, such as the concentration of a PrEP medicine to infer whether black women are protected. An alternative
that has been proposed for men who have sex with men would be to look for other markers of high risk, such as sexually transmitted infections, reported partners, age, and substance use and estimate the likely risk of HIV acquisition in the absence of PrEP from these parameters. Then the observed incidence could be compared to this modelled counterfactual, much as was done in the open label extension of the Partners PrEP study in Kenyan and Ugandan sero-different couples. However, translating risk factors for infection across populations, and even continents when there is such heterogeneity in risk of infection is not at all straightforward. So there is still plenty to think about and no clear answers yet!

A useful addition to the tool box for designing studies and assessing the effectiveness of interventions, would be better tools for measuring recent infection. There are several assays all with differing characteristics but increasingly these differences and how they interact with different clades of HIV are becoming clear. Key determinants for each assay are the mean duration of recent infection (MDRI) estimate (which does seem to vary by clade) and the false recency rate (FRR) which needs to be less than 2% to be considered useful. Hargrove and colleagues used three different assays to test samples from 101 women who seroconverted during the ZVITAMBO trial. The MDRI measured using standard cut-off points, were considerably shorter than those published for the general population. The authors point out that changes in antibody properties among women who have recently given birth or other unspecified physiological states, mean that incidence assays may give different results from those published and expected. Yet more caution when comparing incidence estimates between studies. As an endpoint in a comparison between two groups in the same population, the assays are still attractive. Although, given typical MRDIs of around six to nine months, these assays will still need to be embedded in very large samples to give reliable estimates of incidence and statistically significant differences between groups.

This month saw the production of a useful supplement on many aspects of how data from different sources, including incidence assays are used to inform the sophisticated models on which so much HIV planning, programming and financing is based. An example is Mahiane and colleagues’ paper on the development of a new tool to fit existing programme data into the spectrum suite of models in order to estimate incidence.

Finally in this section, for those who are keen on laboratory studies, Richardson-Harman and colleagues describe the current state of ex-vivo challenge models for assessing potential candidates as microbicides. In these models, biopsies of rectal, cervical or vaginal tissue, taken during other procedures, or from volunteers, are kept alive in the laboratory. The tissues can then be challenged with HIV in the presence or absence of potential microbicide products. The current model works best for rectal tissues, in which infection occurs promptly and consistently, so that the effect of a microbicide can clearly be seen by a reduction in the production of HIV p24 antigen. However, for cervical and vaginal tissues, the infection (in the absence of any microbicide) was less consistent, slower and lasted longer making it less easy to determine statistical differences between those tissues with microbicide and those without. Further work of this sort may help to streamline the choice of microbicide or PrEP products that can most sensibly be taken out of the laboratory and into the (almost) real world of clinical trials.

Small-group randomized controlled trial to increase condom use and HIV testing among Hispanic/Latino gay, bisexual, and other men who have sex with men.

Objectives: To evaluate the HOLA en Grupos intervention, a Spanish-language small-group behavioral HIV prevention intervention designed to increase condom use and HIV testing among Hispanic/Latino gay, bisexual, and other men who have sex with men.

Methods: In 2012 to 2015, we recruited and randomized 304 Hispanic/Latino men who have sex with men, aged 18 to 55 years in North Carolina, to the 4-session HOLA en Grupos intervention or an attention-equivalent general health education comparison intervention. Participants completed structured assessments at baseline and 6-month follow-up. Follow-up retention was 100%.

Results: At follow-up, relative to comparison participants, HOLA en Grupos participants reported increased consistent condom use during the past 3 months (adjusted odds ratio [AOR] = 4.1; 95% confidence interval [CI] = 2.2, 7.9; P < .001) and HIV testing during the past 6 months (AOR = 13.8; 95% CI = 7.6, 25.3; P < .001). HOLA en Grupos participants also reported increased knowledge of HIV (P < .001) and sexually transmitted infections (P < .001); condom use skills (P < .001), self-efficacy (P < .001), expectancies (P < .001), and intentions (P < .001); sexual communication skills (P < .01); and decreased fatalism (P < .001).

Conclusions: The HOLA en Grupos intervention is efficacious for reducing HIV risk behaviors among Hispanic/Latino men who have sex with men.

Abstract access


The reduction in HIV diagnoses in London in 2016 is attributed to pre-exposure prophylaxis (PrEP). We believe that the causes of the 42% decline seen at our clinic are likely to be multifactorial. 56 Dean Street diagnoses one in four of London’s HIV cases, 50% of whom have incident infection (ie, within 4 months of infection). Because of this, and following the results of the START study, we actively recommend treatment at, or close to, diagnosis, reducing the risk of transmission in people who would otherwise be highly infectious.

Abstract access

US black women and HIV prevention: time for new approaches to clinical trials.


Black women bear the highest burden of HIV infection among US women. Tenofovir/emtricitabine HIV prevention trials among women in Africa have yielded varying results. Ideally, a randomized controlled trial (RCT) among US women would provide data for guidelines for US women's HIV pre-exposure prophylaxis use. However, even among US black women at high risk for HIV infection, sample size requirements for an RCT with HIV incidence as its outcome are prohibitively high. We propose to circumvent this large sample size requirement by evaluating relationships between HIV incidence and drug concentrations measured among participants in traditional phase 3 trials in high incidence settings - and then applying these observations to drug concentrations measured among at risk individuals in lower incidence settings, such as
US black women. This strategy could strengthen the evidence base to enable black women to fully benefit from prevention research advances and decrease racial disparities in HIV rates.

Abstract access

Heightened HIV antibody responses in postpartum women as exemplified by recent infection assays: implications for incidence estimates.


Laboratory assays that identify recent HIV infections are important for assessing impacts of interventions aimed at reducing HIV incidence. Kinetics of HIV humoral responses can vary with inherent assay properties, and between HIV subtypes, populations, and physiological states. They are important in determining mean duration of recent infection (MDRI) for antibody-based assays for detecting recent HIV infections. We determined MDRIs for multi-subtype peptide representing subtypes B, E and D (BED)-capture enzyme immunoassay, limiting antigen (LAg), and Bio-Rad Avidity Incidence (BRAI) assays for 101 seroconverting postpartum women, recruited in Harare from 1997 to 2000 during the Zimbabwe Vitamin A for Mothers and Babies trial, comparing them against published MDRIs estimated from seroconverting cases in the general population. We also compared MDRIs for women who seroconverted either during the first 9 months, or at later stages, postpartum. At cutoffs (C) of 0.8 for BED, 1.5 for LAg, and 40% for BRAI, estimated MDRIs for postpartum mothers were 192, 104, and 144 days, 33%, 32%, and 52% lower than published estimates of 287, 152 and 298 days, respectively, for clade C samples from general populations. Point estimates of MDRI values were 7%-19% shorter for women who seroconverted in the first 9 months postpartum than for those seroconverting later. MDRI values for three HIV incidence biomarkers are longer in the general population than among postpartum women, particularly those who recently gave birth, consistent with heightened immunological activation soon after birth. Our results provide a caution that MDRI may vary significantly between subjects in different physiological states.

Abstract access

Improvements in Spectrum's fit to program data tool.


Objective: The Joint United Nations Program on HIV/AIDS-supported Spectrum software package (Glastonbury, Connecticut, USA) is used by most countries worldwide to monitor the HIV epidemic. In Spectrum, HIV incidence trends among adults (aged 15-49 years) are derived by either fitting to seroprevalence surveillance and survey data or generating curves consistent with program and vital registration data, such as historical trends in the number of newly diagnosed infections or people living with HIV and AIDS related deaths. This article describes development and application of the fit to program data (FPD) tool in Joint United Nations Program on HIV/AIDS’ 2016 estimates round.

Methods: In the FPD tool, HIV incidence trends are described as a simple or double logistic function. Function parameters are estimated from historical program data on newly reported HIV cases, people living with HIV or AIDS-related deaths. Inputs can be adjusted for proportions undiagnosed or
misclassified deaths. **Maximum likelihood estimation or minimum chi-squared distance methods are used to identify the best fitting curve. Asymptotic properties of the estimators from these fits are used to estimate uncertainty.**

**Results:** The FPD tool was used to fit incidence for 62 countries in 2016. Maximum likelihood and minimum chi-squared distance methods gave similar results. A double logistic curve adequately described observed trends in all but four countries where a simple logistic curve performed better.

**Conclusion:** Robust HIV-related program and vital registration data are routinely available in many middle-income and high-income countries, whereas HIV seroprevalence surveillance and survey data may be scarce. In these countries, the FPD tool offers a simpler, improved approach to estimating HIV incidence trends.

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**Abstract access**

**Analytical advances in the ex vivo challenge efficacy assay.**


The ex vivo challenge assay is being increasingly used as an efficacy endpoint during early human clinical trials of HIV prevention treatments. There is no standard methodology for the ex vivo challenge assay, although the use of different data collection methods and analytical parameters may impact results and reduce the comparability of findings between trials. In this analysis, we describe the impact of data imputation methods, kit type, testing schedule and tissue type on variability, statistical power, and ex vivo HIV growth kinetics. Data were p24 antigen (pg/ml) measurements collected from clinical trials of candidate microbicides where rectal (n = 502), cervical (n = 88), and vaginal (n = 110) tissues were challenged with HIV-1BaL ex vivo.

Imputation of missing data using a nonlinear mixed effect model was found to provide an improved fit compared to imputation using half the limit of detection. The rectal virus growth period was found to be earlier and of a relatively shorter duration than the growth period for cervical and vaginal tissue types. On average, only four rectal tissue challenge assays in each treatment and control group would be needed to find a one log difference in p24 to be significant (alpha = 0.05), but a larger sample size was predicted to be needed for either cervical (n = 21) or vaginal (n = 10) tissue comparisons. Overall, the results indicated that improvements could be made in the design and analysis of the ex vivo challenge assay to provide a more standardized and powerful assay to compare efficacy of microbicide products.

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**4. Key populations**

*We still lack good data on many specific populations that are most severely affected by HIV*

**Editor’s notes:** Transgender women are often under-represented in HIV research. Yet they face many challenges in day to day life with discrimination at many levels. Employment opportunities are few and many transgender women make a living through sex work. It is well recognized that they are
at specific and increased risks of HIV. Yet many intervention trials group them with gay men and other men who have sex with men, often meaning that the results cannot be disaggregated into more meaningful categories. The number of transgender women in particular studies is also often too small to make strong conclusions from the data they provide to the study. So it is encouraging to see Grinsztejn and colleagues establishing a major study specifically in the community of transgender women in Rio de Janeiro, Brazil. The authors recruited 345 transgender women through a respondent driven sampling process. This non-random approach is necessitated by the nature of the population, as it would not be possible to make a complete sampling frame from census or other documentation. However, statistical approaches to make best estimates of population measures are available and the authors found that almost one third of the women were living with HIV and that 29% had not previously been tested for HIV. The high frequency of other sexually transmitted infections highlights the need for better engagement and services not just for HIV but for their wider sexual and reproductive health and rights needs.

Another population that is under-researched is people with disabilities. “There is a tribe of Ugandans . . . whose issues and needs have not been given their due and appropriate attention in the fight. By all indications, persons with disabilities have been forgotten, consciously and unconsciously. They represent the forgotten tribe” (Mwesigwa Martin Babu, 2005). Abimanyi-Ochom and colleagues used data collected during the 2011 Ugandan demographic and health survey, which included questions about disabilities for the first time. While HIV knowledge is similar in those with and without disabilities, people living with disabilities reported indicators of increased risk of acquiring HIV. Findings included slightly earlier sexual debut and a higher frequency of reported sexually transmitted infections. Other studies have demonstrated that people living with disabilities may have lower self-esteem and self-efficacy and that abuse, including sexual abuse is more common among this group than among their peers.

The findings are reinforced by a study from Cameroon. De Beaudrap and colleagues used the same questionnaire that had been used in the Uganda DHS (the Washington short set of questions on disability) to identify people living with disability in a random sample of the population in Yaounde. The prevalence of HIV was almost twice as high among those with disability than among controls matched by age, sex and residential area. In line with the discussion in the Ugandan paper, the authors in Cameroon found that women with disability were more likely to receive money for sex and to be victims of sexual violence. Both of these characteristics were, not surprisingly, associated with still higher rates of HIV infection. Both papers call for more and better data and we also need to develop and test interventions to reduce the burden of HIV among those living with disabilities.

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


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

Methods: We recruited transwomen from Rio de Janeiro, Brazil, by respondent-driven sampling. Eligibility criteria were self-identification as transwomen, being 18 years of age or older, living in Rio de Janeiro or its metropolitan area, and having a valid peer recruitment coupon. We recruited 12 seed participants from social movements and formative focus groups.
who then used peer recruitment coupons to refer subsequent peers to the study. We categorised participants as HIV negative, known HIV infected, or newly diagnosed as HIV infected. We assessed predictors of newly diagnosed HIV infections by comparing newly diagnosed with HIV-negative participants. We derived population estimates with the Respondent-Driven Sampling II estimator.

Findings: Between Aug 1, 2015, and Jan 29, 2016, we enrolled 345 eligible transwomen. 29·1% (95% CI 23·2-35·4) of participants had no previous HIV testing (adjusted from 60 participants), 31·2% (18·8-43·6) had HIV infections (adjusted from 141 participants), and 7·0% (0·0-15·9) were newly diagnosed as HIV infected (adjusted from 40 participants). We diagnosed syphilis in 28·9% (18·0-39·8) of participants, rectal chlamydia in 14·6% (5·4-23·8), and gonorrhoea in 13·5% (3·2-23·8). Newly diagnosed HIV infections were associated with black race (odds ratio 22·8 [95% CI 2·9-178·9]; p=0·003), travesti (34·1 [5·8-200·2]; p=0·0001) or transsexual woman (41·3 [6·3-271·2]; p=0·0001) gender identity, history of sex work (30·7 [3·5-267·3]; p=0·002), and history of sniffing cocaine (4·4 [1·4-14·1]; p=0·01).

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

Abstract access

HIV/AIDS knowledge, attitudes and behaviour of persons with and without disabilities from the Uganda demographic and health survey 2011: differential access to HIV/AIDS information and services.


Uganda is among the first to use the Washington Group Short Set of Questions on Disability to identify persons with disabilities in its Demographic and Health Survey. In this paper, we review the HIV knowledge, attitudes and behaviour component of the 2011 Ugandan demographic and health survey, analysing a series of questions comparing those with and without disabilities in relation to HIV/AIDS knowledge, attitudes and practices. We found comparable levels of knowledge on HIV/AIDS for those with and those without disabilities in relation to HIV transmission during delivery (93.89%, 93.26%) and through breastfeeding (89.91%, 90.63%), which may reflect increased attention to reaching the community of persons with disabilities. However, several gaps in the knowledge base of persons with disabilities stood out, including misconceptions of risk of HIV infection through mosquito bites and caring for a relative with HIV in own household (34.39%, 29.86%; p<0.001; 91.53%, 89.00%; p = 0.001, respectively). The issue is not just access to appropriate information but also equitable access to HIV/AIDS services and support. Here we found that persons with multiple disabilities were less likely than individuals without disabilities to return to receive results from their most recent HIV test (0.60[0.41-0.87], p<0.05). HIV testing means little if people do not return for follow-up to know their HIV status and, if necessary, to be connected to available services and supports. Additional findings of note were that persons with disabilities reported having a first sexual encounter at a slightly younger age than peers without disabilities; and persons with disabilities also reported having a sexually transmitted disease (STD) within the last 12 months at significantly higher rates than peers without disabilities (1.38[1.18-1.63], p<0.01), despite reporting comparable knowledge of the need for safer sex practices. This analysis is among the first to use HIV/AIDS-related questions from Demographic Health Surveys to
provide information about persons with disabilities in Uganda in comparison to those without disabilities. These findings present a more complex and nuanced understanding of persons with disabilities and HIV/AIDS. If persons with disabilities are becoming sexually active earlier, are more likely to have an STD within the preceding 12 month period and are less likely to receive HIV test results, it is important to understand why. Recommendations are also made for the inclusion of disability measures in Uganda’s AIDS Indicator Survey to provide cyclical and systematic data on disability and HIV/AIDS, including HIV prevalence amongst persons with disabilities.

Abstract

Prevalence of HIV infection among people with disabilities: a population-based observational study in Yaoundé, Cameroon (HandiVIH).


Background: In resource-limited settings, people with disabilities have been left behind in the response to HIV. In the HandiVIH study, we estimate and compare HIV prevalence and associated risk factors between people with and without disabilities.

Methods: In this cross-sectional, population-based, observational study, we used two-phase random sampling to recruit adults with disabilities and a control group matched for age, sex, and residential location from households of the general population. We used the Washington Group Short Set of Questions on Disability to identify people with disabilities. We administered an HIV test and a life-course history interview to participants. The primary outcome was the prevalence of HIV among participants with and without disabilities.

Findings: Between Oct 2, 2014, and Nov 30, 2015, we recruited 807 people with disabilities and 807 participants without disabilities from Yaoundé, Cameroon. 28 of 716 people in the control population had a positive HIV test result (crude prevalence 3·9%, 95% CI 2·9-5·3) compared with 50 of 739 people with disabilities (6·8%, 5·0-8·6; conditional odds ratio [OR] 1·7; p=0·04). Women with disabilities were more often involved in paid sexual relationships than were women without disabilities (2·5% vs 0·5%, p=0·05). People with disabilities were also at increased risk of sexual violence than were women without disabilities (11·0% vs 7·5%, OR 1·5; p=0·01). Sexual violence and sex work were strongly associated with increased risk of HIV infection among participants with disabilities but not among controls (OR 3·0, 95% CI 1·6-5·6 for sexual violence and 12·3, 4·4-34·6 for sex work). Analyses were done in men and women.

Interpretation: The higher prevalence of HIV infection in people with disabilities than people without disabilities reflects a higher exposure to HIV infection as well as the presence of disability-associated HIV infection. The susceptibility of people with disabilities to HIV infection seems to be shaped by social and environmental factors. Research is needed to inform firm recommendations on how to protect this vulnerable population.

5. Elimination of stigma
Short and sweet? Do study participants prefer shorter or longer consent forms? Do they understand the contents?

Editor’s notes: As described above in the HOLA en Grupos study, engagement and partnership is vital if HIV research is to produce useful and relevant results. The ethics of research involving human subjects continues to evolve but the key principles laid out by Beauchamp and Childress in 1989 remain central. The principles of autonomy, non-maleficence, beneficence, and justice, have been extremely influential in the field of medical ethics, and are fundamental for understanding the current approach to ethical assessment in health care.

Autonomy implies that research participants should be able to consent willingly to join a research study and a key part of that informed consent process is usually a written “consent form” that is signed by the participant. However, a major challenge is often to ensure that on the one hand all relevant information about possible benefits and harms is included in the information and on the other hand that the consent process is manageable and appropriate for the participant.

In the largest study of its kind to date, Grady and colleagues embedded a randomized trial within the larger randomized START trial (comparing immediate with deferred start of antiretroviral medicines in people with early HIV infection). Around 4000 participants in START were allocated according to their 154 research sites, which were randomly assigned to the original, lengthy and somewhat complicated consent form, or to a simplified, shorter consent form with much more attention paid to ease of comprehension and readability. The shorter form was still around 1800 words long (compared to the almost 6000 of the original) and was only a little easier to read, because the sponsors of the study needed to be certain that all the information demanded by current guidelines was included.

Surprisingly, there was no overall difference in either the primary outcome (an understanding that participants’ treatment would be randomly allocated) or in overall comprehension of aspects of the study. In other words, the authors did NOT find the advantages that they were expecting from the modified consent form.

However, various clear trends emerge from the data that are relevant to future research too. Those with less education were clearly less able to understand the randomization approach. 73% of the 1240 participants who had not attended high school compared to more than 90% of the 935 who had completed a university degree or postgraduate education answered the primary question on randomization correctly. The START study team were diligent in explaining the study to potential participants before presenting the informed consent form, with around a half of participants reporting more than an hour of explanation prior to being asked for consent, and more than 80% of sites reporting that participants understood the study “very well” prior to the consent process. There was also a clear trend for participants from sites that had been involved in previous HIV research to understand the process better (rising from 69% in those with no previous HIV studies to 85% in those with more than 10).

Increasingly HIV prevention researchers are aiming to work with populations that have high ongoing incidence of HIV. In a world where treatment is increasingly widespread and overall numbers of infections have fallen somewhat, this means that researchers will tend to be working with more and more disadvantaged populations where many participants may be less well educated and less familiar with research. This important study makes it clear that the ethical principle of autonomy requires an ongoing process that goes far beyond the choice of words in a consent form. Research must build trust between researchers and participants. The research team should explain carefully and in appropriate ways what is involved in the study and what options participants have. Study teams should build a governance process into the research so that participants can have confidence that any risks of the research, both for them as individuals, but also often for the community or group to
which they belong, are monitored and mitigated. In this way potentially vulnerable individuals may still be recruited into important research projects and contribute to the ways in which science can end the epidemic.

A randomized trial comparing concise and standard consent forms in the START trial.


Background: Improving the effectiveness and efficiency of research informed consent is a high priority. Some express concern about longer, more complex, written consent forms creating barriers to participant understanding. A recent meta-analysis concluded that randomized comparisons were needed.

Methods: We conducted a cluster-randomized non-inferiority comparison of a standard versus concise consent form within a multinational trial studying the timing of starting antiretroviral therapy in HIV+ adults (START). Interested sites were randomized to standard or concise consent forms for all individuals signing START consent. Participants completed a survey measuring comprehension of study information and satisfaction with the consent process. Site personnel reported usual site consent practices. The primary outcome was comprehension of the purpose of randomization (pre-specified 7.5% non-inferiority margin).

Results: 77 sites (2429 participants) were randomly allocated to use standard consent and 77 sites (2000 participants) concise consent, for an evaluable cohort of 4229. Site and participant characteristics were similar for the two groups. The concise consent was non-inferior to the standard consent on comprehension of randomization (80.2% versus 82%, site adjusted difference: 0.75% (95% CI -3.8%, +5.2%)); and the two groups did not differ significantly on total comprehension score, satisfaction, or voluntariness (p>0.1). Certain independent factors, such as education, influenced comprehension and satisfaction but not differences between consent groups.

Conclusions: An easier to read, more concise consent form neither hindered nor improved comprehension of study information nor satisfaction with the consent process among a large number of participants. This supports continued efforts to make consent forms more efficient.

Trial registration: Informed consent substudy was registered as part of START study in clinicaltrials.gov #NCT00867048, and EudraCT # 2008-006439-12.

Abstract Full-text [free] access

6. Health systems and services

Where are we heading with the horrible interaction between human papillomavirus (HPV) and HIV?

Editor's notes: Human papillomavirus (HPV) is the most common sexually transmitted infection in the world. There are over 200 different strains of HPV, distinguished by genetic typing. The strains are classified into high-risk and low-risk based on their associations with the development of cervical cancer, but also genital warts and anal cancer. HPV16 is the most common high-risk strain and is found in about half of cervical cancers and 70% of anal cancers. Although anal cancer is much less
common than cervical cancer among women, there is clear evidence that women living with HIV are at greater risk not only of cervical cancer but also of anal cancer.

In a study in Vitoria, Brazil, Volpini and colleagues collected cervical and anal samples from 126 women living with HIV who had recently had a normal Pap smear, and so did not already have precancerous lesions in the cervix. They found DNA from HPV in 71% of the women. 39% of women had HPV in cervical samples, while 60% had HPV in anal samples.

HPV16 was the most prevalent type at the cervical and anal sites (9% and 18%, respectively). Other high risk strains were found in the cervical samples from more than 30% of women and in the anal samples of another 12% of women (some women had multiple strains). All currently available vaccines protect against HPV16 and one also protects against HPV45 and 31 (which accounted for almost half of the remaining high risk strains from the cervical samples). The vaccine works best when given before any HPV infection, and is therefore recommended for girls before they become sexually active. However, persistence and clearance of HPV is a dynamic process and the possible benefits of vaccination in those already infected are not yet clear.

Testing for HPV is becoming increasingly sophisticated, with molecular technology becoming available that allows detection of DNA and strain typing. It seems very probable that women living with HIV with high-risk strains in either cervical or anal samples are at greater risk of developing cancer and therefore need additional more intense screening to detect and treat any pre-cancerous abnormalities in their epithelium prior to the development of invasive cancers. Current guidelines already recommend that women living with HIV are offered Pap smears more regularly than their HIV-negative peers. DNA based technology may make it possible to offer a more targeted approach to women at the most risk.

In the meantime, encouraging HPV vaccination among schoolgirls (and eventually boys too) is a long term prevention measure. Ensuring that HPV screening services and HIV prevention and care services are well co-ordinated or even integrated is something that will have an immediate impact on preventing deaths from cervical cancer. Incorporating molecular testing might help us to reduce the incidence of anal cancer too.

The high prevalence of HPV and HPV16 European variants in cervical and anal samples of HIV-seropositive women with normal Pap test results.


Human immunodeficiency virus (HIV)-seropositive women are more likely to have anogenital cancer, and high risk-HPV (HR-HPV) infection is the main associated factor. Between August 2013 and December 2015, we conducted a descriptive study to determine the HPV genotypes and HPV16 variants in cervical and anal samples of HIV-seropositive women with a normal Pap test. The viral DNA was amplified by PCR using the PGMY09/11 set of primers. Reverse line blot (RLB), restriction fragment length polymorphism (RFLP) and sequencing assays were used to determine the HPV genotypes. HPV16 variants were identified by gene sequencing. We found a high frequency of HR-HPV (60.3%; 76/126) at the anogenital site among HIV-seropositive women and without association with anal intercourse. HPV16 and European variant predominated among the HR-HPV. Mixed infections with at least three different HPV types were common, particularly at the anal site. CD4+ T-cell counts below 500 cells/mm³, a HIV viral load above 50 copies/mL and an age of 18 to 35 years old were all related to HPV anal infection. Our study showed a high frequency of HR-
HPV in both cervical and anal sites of women with negative cytology belonging to a risk group for the development of anogenital cancer.

Abstract Full-text [free] access