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

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   - Home-based HIV counselling & testing increases uptake of testing in Zambia
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Towards the elimination of travel restrictions for people living with HIV

8. Strengthening HIV integration

- Health system barriers to achieving the potential of integrated service delivery

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UNAIDS
1. Reduce sexual transmission

Effect of home based HIV counselling and testing intervention in rural South Africa: cluster randomised trial.


Objective: To assess the effect of home based HIV counselling and testing on the prevalence of HIV testing and reported behavioural changes in a rural subdistrict of South Africa.

Design: Cluster randomised controlled trial.

Setting: 16 communities (clusters) in uMzimkhulu subdistrict, KwaZulu-Natal province, South Africa.

Participants: 4154 people aged 14 years or more who participated in a community survey.

Intervention: Lay counsellors conducted door to door outreach and offered home based HIV counselling and testing to all consenting adults and adolescents aged 14-17 years with guardian consent. Control clusters received standard care, which consisted of HIV counselling and testing services at local clinics.

Main outcome measures: Primary outcome measure was prevalence of testing for HIV. Other outcomes were HIV awareness, stigma, sexual behaviour, vulnerability to violence, and access to care.

Results: Overall, 69% of participants in the home based HIV counselling and testing arm versus 47% in the control arm were tested for HIV during the study period (prevalence ratio 1.54, 95% confidence interval 1.32 to 1.81). More couples in the intervention arm had counselling and testing together than in the control arm (2.24, 1.49 to 3.03). The intervention had broader effects beyond HIV testing, with a 55% reduction in multiple partners (0.45, 0.33 to 0.62) and a stronger effect among those who had an HIV test (0.37, 0.24 to 0.58) and a 45% reduction in casual sexual partners (0.55, 0.42 to 0.73).

Conclusions: Home based HIV counselling and testing increased the prevalence of HIV testing in a rural setting with high levels of stigma. Benefits also included higher uptake of couple counselling and testing and reduced sexual risk behaviour.

Keywords: Voluntary counselling and testing, home-based

Abstract Full-text [free] access

Editor’s notes: HIV counselling and testing is a first step in accessing prevention and treatment interventions, and there is increasing public health emphasis on couples voluntary counselling and testing (VCT). Recently, the HPTN 043 trial of community-mobilisation and community-based VCT showed a significantly increased uptake of testing compared to facility-based VCT in South Africa and Thailand, especially among men. This paper reports results of a cluster randomised trial undertaken to test the hypothesis that home-based counselling and testing would result in higher uptake than facility based testing, and was set in a rural, high HIV prevalence setting (a subdistrict of Sisonke district in KwaZulu-Natal province, a rural region known for high levels of stigma towards people with HIV/AIDS). Lay female counsellors were trained to conduct HIV counselling and testing through door-to-door visits of all households in the 8 intervention clusters. The intervention had a significant effect on the prevalence of HIV testing, as well as on couple counselling and testing. The prevalence ratio was similar for males and females, with lower uptake among males in both the intervention and control arms (47% uptake among males in the intervention arm vs. 75% among females). There was a significant reduction in reported risky behaviour, including having more than one sexual partner, or a casual partner, in the past 3 months. In contrast, there was no effect on reported condom use at last sex, or in knowledge about HIV (which was high in both arms). The proportion of those tested who were HIV positive was significantly lower in the intervention arm (6% vs. 10%, PR=0.65, 95%CI 0.47-0.90), indicating the opportunity for prevention by promoting earlier testing among HIV negative individuals. Overall, the trial provides evidence that home-
based HIV counselling and testing by lay counsellors paid local salaries is feasible and acceptable, and should be considered for scale-up.

Strong effects of home-based voluntary HIV counselling and testing on acceptance and equity: a cluster randomised trial in Zambia.


Home-based voluntary HIV counselling and testing (HB-VCT) has been reported to have a high uptake, but it has not been rigorously evaluated. We designed a model for HB-VCT appropriate for wider scale-up, and investigated the acceptance of home-based counselling and testing, equity in uptake and negative life events with a cluster-randomized trial. Thirty six rural clusters in southern Zambia were pair-matched based on baseline data and randomly assigned to the intervention or the control arm. Both arms had access to standard HIV testing services. Adults in the intervention clusters were offered HB-VCT by local lay counsellors. Effects were first analysed among those participating in the baseline and post-intervention surveys and then as intention-to-treat analysis. The study was registered with www.controlled-trials.com, number ISRCTN53353725. A total of 836 and 858 adults were assigned to the intervention and control clusters, respectively. In the intervention arm, counselling was accepted by 85% and 66% were tested (n = 686). Among counselled respondents who were cohabiting with the partner, 62% were counselled together with the partner. At follow-up eight months later, the proportion of adults reporting to have been tested the year prior to follow-up was 82% in the intervention arm and 52% in the control arm (Relative Risk (RR) 1.6, 95% CI 1.4-1.8), whereas the RR was 1.7 (1.4-2.0) according to the intention-to-treat analysis. At baseline the likelihood of being tested was higher for women vs. men and for more educated people. At follow-up these differences were found only in the control communities. Measured negative life events following HIV testing were similar in both groups. In conclusion, this HB-VCT model was found to be feasible, with a very high acceptance and to have important equity effects. The high couple counselling acceptance suggests that the home-based approach has a particularly high HIV prevention potential.

Abstract access

Editor’s notes: Like the trial by Doherty et al., this cluster randomised trial was designed to evaluate the impact of home-based VCT (HB-VCT) on uptake of testing by trained lay counsellors in a high HIV prevalence setting. 36 communities in southern Zambia were randomised and followed for 8 months. Uptake of testing was high, and the intervention had a significant effect on the prevalence of HIV testing, with relatively high uptake among men (76% in the intervention arm vs. 42% in the control arm) compared with women (86% in the intervention arm vs. 60% in the control arm). In this setting, uptake of HIV testing is greater among those with more years of education, but the intervention resulted in high levels of HIV testing (>77%) regardless of education level. There was no evidence that HB-VCT was associated with negative life events such as break-up of marriage or relationship, or physical violence. The results of these two similar trials show that a model of using trained lay counsellors for HB-VCT is feasible in certain settings and can achieve high acceptance of testing. Both trials found high levels of couples counselling and testing, unlike previous trials of community-based VCT. In both trials, participants testing HIV positive were referred for treatment and care to a local healthcare facility, and it will be important to see further data on the linkage-to-care following HB-VCT.

Voluntary HIV testing and risky sexual behaviours among health care workers: a survey in rural and urban Burkina Faso.


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Background: Voluntary counselling and testing (VCT) together with a safe sexual behaviour is an important preventive strategy in the control of HIV. Although health care workers (HCWs) are critical in the response to HIV, little is known about VCT and high-risk behaviours (HRB) among this group in West Africa. This study aims to assess the prevalence of VCT and HRB among HCWs in Burkina Faso.

Methods: We collected data through a questionnaire in urban areas (Ouagadougou and Bobo-Dioulasso) and rural areas (Poni and Yatenga) among HCWs from 97 health care facilities. Urine samples were collected, screened for HIV using a Calypte® test kit and confirmed by Western Blot. Multiple logistic regression analysis was performed to identify factors associated with the use of VCT services and with high-risk sex behaviour.

Results: About 92.5% of eligible HCWs participated (1570 out of 1697). Overall, 38.2% of them (34.6% of women and 42.6% of men) had ever used VCT services. About 40% of HCWs reported that fear of knowing the test result was the main reason for not doing the HIV test. Male HCWs (p = 0.001), laboratory workers (p < 0.001), those having two years or more experience (p = 0.03), and those who had multiple partners (p = 0.001) were more likely to have tested for HIV. One fifth of HCWs reported multiple partners. Of these, thirteen percent did not use condoms. HCWs who had multiple partners were significantly more likely to be men, single, living in rural areas, and under the age of 29 years.

Conclusion: VCT was still very low among HCWs in Burkina Faso, while HRB was high. These findings suggest that 'HCW-friendly' VCT centres should be implemented, securing confidentiality among colleagues. In addition, refreshment courses on HIV risk reduction, counselling and testing are certainly required during the professional career of HCWs.

Keywords: VCT, High-risk sex, Health care workers

Abstract

Editor’s notes: Health care workers (HCWs) are central for the management and care of people living with HIV and are at the forefront for informing their patients about HIV and the benefits of HIV testing. There is little data on HIV testing among this key occupational group. This large cross-sectional study is the first to investigate uptake of VCT services and sexual behaviour among HCWs in a representative sample in West Africa. The sample included nurses, midwives, students, administrative and manual workers, and laboratory workers. Laboratory workers were most likely to have been tested (83%), and administrative/manual workers least likely (25%). The questionnaire was self-administered so potentially subject to some bias such as underreporting of socially unacceptable behaviours but the results are interesting as they show that despite this occupational group having access to knowledge on HIV prevention and the benefits of HIV testing, around a quarter reported having engaged in risky behaviour in the past year, and less than half of them used a VCT centre. Qualitative research is necessary to better understand this paradoxical behaviour. It would be interesting to link these findings with the attitude of HCWs for promoting VCT and informing patients on risk behaviour in order to assess training needs and opportunities for HIV risk reduction for this target population.

Female sex work interventions and changes in HIV and syphilis infection risks from 2003 to 2008 in India: a repeated cross-sectional study


Objectives: We examined if increased spending and coverage of female sex worker (FSW) interventions were associated with declines in HIV or syphilis risk among young pregnant women (as a proxy for new infections in the general population) in the high-burden southern states of India.

Design: Repeated cross-sectional analysis.

Setting: We used logistic regression to relate district-level spending, number of sexually transmitted infections (STIs) treated, FSWs reached or condoms distributed to the declines in the annual risk of HIV and syphilis from
2003 to 2008 among prenatal clinic attendees in the four high-HIV burden states of Andhra Pradesh, Karnataka, Maharashtra and Tamil Nadu.

Participants: 386,961 pregnant women aged 15-24 years (as a proxy for incident infections in the adult population).

Interventions: We examined National AIDS Control Organisation (NACO) data on 868 FSW intervention projects implemented between 1995 and 2008.

Primary and secondary outcome measures: HIV or syphilis infection.

Results: HIV and syphilis prevalence declined substantially among young pregnant women. Each additional STI treated (per 1000 people) reduced the annual risk of HIV infection by -1.7% (95% CI -3.3 to -0.1) and reduced the annual risk of syphilis infection by -10.9% (95% CI -15.9 to -5.8). Spending, FSWs reached or condoms distributed did not reduce HIV risk, but each was significantly associated with reduced annual risk of syphilis infection. There were no major differences between the NACO-funded and Avahan-funded districts in the annual risk of either STI.

Conclusions: Targeted FSW interventions are associated with reductions in syphilis risk and STI treatment is associated with reduced HIV risk. Both more and less costly FSW interventions have comparable effectiveness.

Keywords: Infectious Diseases, Public Health

Abstract Full-text [free] access

Editor’s notes: This study utilizes data from the large-scale interventions targeted at female sex workers (FSW) in southern India by the Indian Government’s National AIDS Control Organisation (NACO) (1995-2008), and the Gates Foundation Avahan programme (2004 onwards). The authors link FSW intervention spending and coverage to unlinked anonymous HIV and syphilis status in almost 400,000 antenatal clinic attendees aged 15-24 years from 2003-2008. During this period, there were significant decreases in both HIV and syphilis risk. The decline in risk of both syphilis and HIV was inversely correlated with rate of STI treatment. In addition, the decline in syphilis risk was significantly associated with the intervention coverage and spending. The strong association with STI treatment underscores the need to maintain a focus on STD treatment to reduce risk of HIV transmission, especially in settings where core epidemiological groups, such as FSW, have high prevalence of STD, in order to interrupt STI transmission from FSW to their male clients, and onwards to the general female population.

2. 15 million accessing treatment

Development of a diagnosis disclosure model for perinatally HIV-infected children in Thailand.


While disclosure of HIV status to perinatally HIV-infected children has become an increasingly important clinical issue, specific disclosure guidelines are lacking. We developed a pediatric HIV diagnosis disclosure model to support caretakers. All HIV-infected children greater than 7-years-old at two participating hospitals in Bangkok, Thailand, and their caretakers, were offered disclosure according to the 4-step protocol: (1) screening; (2) readiness assessment; (3) disclosure; and (4) follow-up. Disclosure occurred after agreement of both providers and caretakers. Among 438 children who were screened, 398 (89%) were eligible. Readiness assessment was completed for 353 (89%) of eligible children and 216 (61%) were determined ready. Disclosure was done for 186 children. The mean age at eligibility screening was 10.5 years (range: 6.8-15.8 years); the mean age at disclosure was 11.7 years (range: 7.6-17.7 years). The mean duration between eligibility screening and disclosure was 15.2 months. There were no significant negative behavioral or emotional
outcomes reported in children following disclosure. This HIV diagnosis disclosure model was feasible to implement and had no negative outcomes. As the time for preparation process was over 1 year for most cases, the disclosure process can be initiated as early as age 7 to allow enough time for disclosure to be completed by the age of adolescence.

Abstract access

Editor’s notes: Increasing numbers of HIV-infected children are now surviving into adolescence because of antiretroviral therapy. While disclosure to children of their HIV diagnosis is known to be crucial, this process is very often delayed because caretakers find the process difficult. In this study, caretakers disclosed to children with support from a care provider before, during and after disclosure. There were no negative consequences for children once they knew their diagnosis, although the study was not able to determine if this model had any impact on longer-term adherence and psychosocial status. This care-taker assisted disclosure model provides a practical, systematic and stepwise guide to facilitate paediatric disclosure, as well as being adaptable to the caretakers’ wishes and children’s needs. Preparing the caretaker to disclose can take a long time and care providers should initiate this process when the child is as young as 7 years, to enable disclosure to occur before the child reaches adolescence. The disclosure manual is available here.

Failure to initiate antiretroviral therapy, loss to follow-up and mortality among HIV-infected patients during the pre-ART period in Uganda.


Background: Delays and failures in initiation of antiretroviral therapy (ART) among treatment eligible patients may compromise the effectiveness of HIV care in Africa. An accurate understanding, however, of the pace and completeness of ART initiation and mortality during the waiting period is obscured by frequent losses to follow-up.

Methods: We evaluated newly ART-eligible HIV-infected adults from 2007 to 2011 in a prototypical clinic in Mbarara, Uganda. A random sample of patients lost to follow-up was tracked in the community to determine vital status and ART initiation after leaving the original clinic. Outcomes among the tracked patients were incorporated using probability weights, and a competing risks approach was used in analyses.

Results: Among 2633 ART-eligible patients, 490 were lost to follow-up, of whom a random sample of 132 was tracked and 111 (84.0%) had outcomes ascertained. After incorporating the outcomes among the lost, the cumulative incidence of ART initiation at 30, 90, and 365 days after eligibility was 16.0% [95% confidence interval (CI): 14.2 to 17.7], 64.5% (95% CI: 60.9 to 68.1), and 81.7% (95% CI: 77.7 to 85.6). Death before ART was 7.7% at 1 year. Male sex, higher CD4 count, and no education were associated with delayed ART initiation. Lower CD4 level, malnourishment, and travel time to clinic were associated with mortality.

Conclusions: Using a sampling-based approach to account for losses to follow-up revealed that both the speed and the completeness of ART initiation were suboptimal in a prototypical large clinic in Uganda. Improving the kinetics of ART initiation in Africa is needed to make ART more in real-world populations.

Abstract access

Editor’s notes: Weaknesses in the HIV care pathway undermine the effectiveness of ART at an individual and population level. This study from Uganda examined one step in the overall pathway – the initiation of ART among people with HIV (median CD4 count, 131 cells/μL) identified as eligible to start treatment (CD4<250 cells/μL). High rates of ascertainment of patients lost to follow-up, by careful tracking of a sample of patients within the community, permitted a much clearer evaluation of ART uptake and mortality during the period before starting ART. At 60 days only 50% of eligible patients had started ART. 1 in 5 did
not start ART within 1 year of eligibility and 1 in 12 died before starting ART. Improvements to the implementation strategy are needed.

Factors associated with loss to clinic among HIV patients not yet known to be eligible for antiretroviral therapy (ART) in Mozambique.


Introduction: Retention in HIV care prior to ART initiation is generally felt to be suboptimal, but has not been well-characterized.

Methods: We examined data on 37,352 adult pre-ART patients (ART ineligible or unknown eligibility) who enrolled in care during 2005-2008 with >1 clinical visit at 23 clinics in Mozambique. We defined loss to clinic (LTC) as >12 months since the last visit among those not known to have died/transfered. Cox proportional-hazards models were used to examine factors associated with LTC, accounting for clustering within sites.

Results: Of 37,352 pre-ART patients, 61% had a CD4 count within three months of enrolment (median CD4: 452, IQR: 345-611). 17,598 (47.1%) were ART ineligible and 19,754 (52.9%) were of unknown eligibility status at enrolment because of missing information on CD4 count and/or WHO stage. Kaplan-Meier estimates for LTC at 12 months were 41% (95% CI: 40.2-41.8) and 48% (95% CI: 47.2-48.8), respectively. Factors associated with LTC among ART ineligible patients included male sex (AHRmen_vs_non-pregnant women: 1.5; 95% CI: 1.4-1.6) and being pregnant at enrolment (AHRpregnant_vs_non-pregnant women: 1.3; 95% CI: 1.1-1.5). Older age, more education, higher weight and more advanced WHO stage at enrolment were independently associated with lower risks of LTC. Similar findings were observed among patients whose ART eligibility status was unknown at enrolment.

Conclusions: Substantial LTC occurred prior to ART initiation among patients not yet known to be eligible for ART, including nearly half of patients without documented ART eligibility assessment. Interventions are needed to target pre-ART patients who may be at higher risk for LTC, including pregnant women and patients with less advanced HIV disease.

Abstract Full-text [free] access

Editor’s notes: Weaknesses in the HIV care pathway undermine the effectiveness of ART at an individual and population level. This study from Mozambique assessed losses to clinical care among 37,352 patients who were either (a) not yet eligible for ART or (b) eligibility was not yet known. 39% did not have a CD4 count measurement within 3 months; those who did tended to have high CD4 counts. Extremely high losses to care (almost half the patients) were documented among both groups of patients, and risk factor analysis highlighted male sex, young age (15-25 years) and pregnancy. Pre-ART care for those not yet eligible / known to be eligible for ART needs strengthening hugely.

Disengagement from care in a decentralised primary health care antiretroviral treatment programme: cohort study in rural South Africa.


Objective: To determine rates of, and factors associated with, disengagement from care in a decentralised antiretroviral programme.

Methods: Adults (≥16 years) who initiated antiretroviral therapy (ART) in the Hlabisa HIV Treatment and Care Programme August 2004-March 2011 were included. Disengagement from care was defined as no clinic visit for 180 days, after adjustment for mortality. Cumulative incidence functions for disengagement from care, stratified by year of ART initiation, were obtained; competing-risks regression was used to explore factors associated with disengagement from care.
Results: A total of 4,674 individuals (median age 34 years, 29% male) contributed 13,610 person-years of follow-up. After adjustment for mortality, incidence of disengagement from care was 3.4 per 100 person-years (95% confidence interval (CI) 3.1-3.8). **Estimated retention at 5 years was 61%**. The risk of disengagement from care increased with each calendar year of ART initiation (P for trend <0.001). **There was a strong association between disengagement from care and higher baseline CD4+ cell count** (subhazard ratio (SHR) 1.94 (P < 0.001) and 2.35 (P < 0.001) for CD4+ cell count 150-200 cells/μl and >200 cells/μl respectively, compared with CD4 count <50 cells/μl). Of those disengaged from care with known outcomes, the majority (206/303, 68.0%) remained resident within the local community.

Conclusions: **Increasing disengagement from care threatens to limit the population impact of expanded antiretroviral coverage**. The influence of both individual and programmatic factors suggests that alternative service delivery strategies will be required to achieve high rates of long-term retention.

**Abstract**

**Editor’s notes:** With WHO guidelines now recommending initiation of ART at a CD4 count of 500 or below, health services will need to retain increasing numbers of patients on ART. In many programmatic settings, deaths among people on ART are under-reported, and many people who are recorded as lost to follow-up have in reality died.

This study, in a rural area in South Africa with a well-established demographic surveillance system, had unusually good data on deaths, and so these data on people disengaged from care (defined as those lost to follow up but excluding deaths) are more accurate than is usually possible. Higher CD4 count at ART initiation was associated with disengagement from care. This raises concerns about retention as ART is started at higher CD4 counts and about the effectiveness at population of an “ART treatment as prevention” strategy where people start ART regardless of CD4 count. It is notable that among those disengaged from care, almost 10% subsequently died. Strategies to support retention in ART care are needed, and may be more important for people starting ART at earlier stages of HIV disease.

Ritonavir-boosted lopinavir plus nucleoside or nucleotide reverse transcriptase inhibitors versus ritonavir-boosted lopinavir plus raltegravir for treatment of HIV-1 infection in adults with virological failure of a standard first-line ART regimen (SECOND-LINE): a randomised, open-label, non-inferiority study.


Background: Uncertainty exists about the best treatment for people with HIV-1 who have virological failure with first-line combination antiretroviral therapy of a non-nucleoside analogue (NNRTI) plus two nucleoside or nucleotide analogue reverse transcriptase inhibitors (NtRTI). We compared a second-line regimen combining two new classes of drug with a WHO-recommended regimen.

Methods: We did this 96-week, phase 3b/4, randomised, open-label non-inferiority trial at 37 sites worldwide. Adults with HIV-1 who had confirmed virological failure (plasma viral load >500 copies per mL) after 24 weeks or more of first-line treatment were randomly assigned (1:1) to receive ritonavir-boosted lopinavir plus two or three NtRTIs (control group) or ritonavir-boosted lopinavir plus raltegravir (raltegravir group). The randomisation sequence was computer generated with block randomisation (block size four). Neither participants nor investigators were masked to allocation. The primary endpoint was the proportion of participants with plasma viral load less than 200 copies per mL at 48 weeks in the modified intention-to-treat population, with a non-inferiority margin of 12%. This study is registered with ClinicalTrials.gov, number NCT00931463.

Findings: We enrolled 558 patients, of whom 541 (271 in the control group, 270 in the raltegravir group) were included in the primary analysis. At 48 weeks, 219 (81%) patients in the control group compared with 223 (83%) in the raltegravir group met the primary endpoint (difference 1·8%, 95% CI -4·7 to 8·3), fulfilling the
criterion for non-inferiority. 993 adverse events occurred in 271 participants in the control group versus 895 in 270 participants in the raltegravir group, the most common being gastrointestinal.

Interpretation: The raltegravir regimen was no less efficacious than the standard of care and was safe and well tolerated. This simple NtRTI-free treatment strategy might extend the successful public health approach to management of HIV by providing simple, easy to administer, effective, safe, and tolerable second-line combination antiretroviral therapy.

Abstract access

Editor's notes: In resource-limited settings patients with first-line treatment failure are increasingly encountered. This non-inferiority trial randomised patients with virological failure (defined as 2xVL>500 copies/ml) to WHO recommended second-line ART (ritonavir boosted protease inhibitor [bPI] plus 2 or 3 NRTIs) or a regimen containing two new drug classes (ritonavir bPI plus the integrase inhibitor raltegravir). The results show that both regimens were efficacious. However, there was a trend towards more adverse events in patients on the WHO recommended regimen.

This trial was designed to assess efficacy - a strict definition of virological failure was used (2xVL>500 copies/ml) and the majority of patients had access to resistance tests to guide choice of NRTI backbone. However, recent data from a trial in sub-Saharan Africa, in programmes without access to routine viral load monitoring, support the finding that raltegravir / bPI regimens are as efficacious as current WHO-recommended second-line ART (Paton et al, EARNEST trial, IAS 2013). The raltegravir-based regimen has a number of potential advantages – it is NRTI-sparing, is well tolerated by patients and is simple to administer. In addition the use of two new drug classes removes the need for resistance tests prior to switch. Its major disadvantage is cost, which at current prices would prohibit its widespread use. Finally, further consideration needs to be given to the sequencing of regimens: should raltegravir be used in second-line ART or saved for third-line regimens?

Nucleoside reverse transcriptase inhibitor resistance mutations associated with first-line stavudine-containing antiretroviral therapy: programmatic implications for countries phasing out stavudine.


Background: The World Health Organization Antiretroviral Treatment Guidelines recommend phasing-out stavudine because of its risk of long-term toxicity. There are two mutational pathways of stavudine resistance with different implications for zidovudine and tenofovir cross-resistance, the primary candidates for replacing stavudine. However, because resistance testing is rarely available in resource-limited settings, it is critical to identify the cross-resistance patterns associated with first-line stavudine failure.

Methods: We analyzed HIV-1 resistance mutations following first-line stavudine failure from 35 publications comprising 1,825 individuals. We also assessed the influence of concomitant nevirapine vs. efavirenz, therapy duration, and HIV-1 subtype on the proportions of mutations associated with zidovudine vs. tenofovir cross-resistance.

Results: Mutations with preferential zidovudine activity, K65R or K70E, occurred in 5.3% of individuals. Mutations with preferential tenofovir activity, ≥ two thymidine analog mutations (TAMs) or Q151M, occurred in 22% of individuals. Nevirapine increased the risk of TAMs, K65R, and Q151M. Longer therapy increased the risk of TAMs and Q151M but not K65R. Subtype C and CRF01_AE increased the risk of K65R, but only CRF01_AE increased the risk of K65R without Q151M.
Conclusions: Regardless of concomitant nevirapine vs. efavirenz, therapy duration, or subtype, tenofovir was more likely than zidovudine to retain antiviral activity following first-line d4T therapy.

Abstract access

Editor’s notes: Due to concerns about long term toxicity the World Health Organization no longer recommends the use of stavudine in first-line, NNRTI-based, antiretroviral therapy. Instead, tenofovir or zidovudine should be substituted. For patients with viral suppression this treatment modification is relatively straight-forward and either drug can be used; however the optimal choice of NRTI backbone for patients who are experiencing virological failure or with unknown viral load status is less clear. This is because mutations accumulate along two distinct pathways in patients failing stavudine-based first-line ART, one of which has implications for the effectiveness of zidovudine and the other for tenofovir.

By using the Stanford HIV Drug Resistance Database and pooling the sequences from 35 previously published studies, this study describes the patterns of cross-mutations amongst 1825 patients failing stavudine-based first-line ART. 5% of patients had K65R or K70E detected, making zidovudine the preferred agent for these patients. In contrast 22% of patients had mutations which would favour the subsequent use of tenofovir (≥2 TAMs or Q151M). Important information which could influence the patterns of cross-resistance mutations was not available for this analysis (e.g. the duration of viraemia at the time of genotyping and previous drug substitutions including prior exposure to zidovudine) therefore these results must be interpreted with a degree of caution. Nevertheless, these findings do favour the use of tenofovir rather than zidovudine, in patients with virological failure on first-line ART, or in whom the virological status is unknown.

Decentralising HIV treatment in lower- and middle-income countries.


Background: Policy makers, health staff and communities recognise that health services in lower- and middle-income countries need to improve people's access to HIV treatment and retention to treatment programmes. One strategy is to move antiretroviral delivery from hospitals to more peripheral health facilities or even beyond health facilities. This could increase the number of people with access to care, improve health outcomes, and enhance retention in treatment programmes. On the other hand, providing care at less sophisticated levels in the health service or at community-level may decrease quality of care and result in worse health outcomes. To address these uncertainties, we summarised the research studies examining the risks and benefits of decentralising antiretroviral therapy service delivery.

Objectives: To assess the effects of various models that decentralised HIV treatment and care to more basic levels in the health system for initiating and maintaining antiretroviral therapy.

Search methods: We conducted a comprehensive search to identify all relevant studies regardless of language or publication status (published, unpublished, in press, and in progress) from 1 January 1996 to 31 March 2013, and contacted relevant organisations and researchers. The search terms included ‘decentralisation’, ‘down referral’, ‘delivery of health care’, and ‘health services accessibility’.

Selection criteria: Our inclusion criteria were controlled trials (randomised and non-randomised), controlled-before and after studies, and cohorts (prospective and retrospective) in which HIV-infected people were either initiated on antiretroviral therapy or maintained on therapy in a decentralised setting in lower- and middle-income countries. We define decentralisation as providing treatment at a more basic level in the health system to the comparator.

Data collection and analysis: Two authors applied the inclusion criteria and extracted data independently. We designed a framework to describe different decentralisation strategies, and then grouped studies against these strategies. Data were pooled using random-effects meta-analysis. Because loss to follow up in HIV
programmes is known to include some deaths, we used **attrition** as our primary outcome, defined as **death plus loss to follow-up**. We assessed **evidence quality** with GRADE methodology.

Main results: **Sixteen studies** met the inclusion criteria, all but one were from Africa, comprising two cluster randomised trials and 14 cohort studies. **Antiretroviral therapy started at a hospital and maintained at a health centre (partial decentralisation) probably reduces attrition** (RR 0.46, 95% CI 0.29 to 0.71, 4 studies, 39 090 patients, moderate quality evidence). There may be fewer patients lost to care with this model (RR 0.55, 95% CI 0.45 to 0.69, low quality evidence). We are uncertain whether there is a difference in attrition for antiretroviral therapy started and maintained at a health centre (full decentralisation) compared to a hospital at 12 months (RR 0.70, 95% CI 0.47 to 1.02; four studies, 56 360 patients, very low quality evidence), but there are probably fewer patients lost to care with this model (RR 0.3, 95% CI 0.17 to 0.54, moderate quality evidence).

When antiretroviral maintenance therapy is delivered at home by trained volunteers, there is probably no difference in attrition at 12 months (RR 0.95, 95% CI 0.62 to 1.46, two trials, 1453 patients, moderate quality evidence).

Authors’ conclusions: Decentralisation of HIV care aims to improve patient access and retention in care. Most data were from good quality cohort studies but confounding between site of treatment and outcomes cannot be excluded. Nevertheless, this review found that **attrition appears to be lower in partial decentralisation models of treatment**, where antiretrovirals were started at hospital and continued in the health centre; with antiretroviral drugs started and continued at **health centres, no difference** in attrition was detected, but there were fewer patients lost to care. For antiretroviral therapy **provided at home by trained volunteers**, no difference in outcomes was detected when compared to facility-based care.

Abstract  Full-text [free] access

**Editor’s notes:** As we aim to reach targets of 15 million people on ART by 2015, there is a great need to expand ART services and make them more accessible and to use models that can be scaled up given the constraints within the health sector. One approach is to decentralise care and provide follow up care to patients in health centres or at home. This is a systematic review of the impact of three models of decentralised care on patient retention; while the two health centre based models appear to significantly improve retention relative to a hospital based model. This provides important evidence the potential of decentralised ART to greatly expand treatment access, in particular to rural areas.

3. Avoid TB deaths

**Time to treatment and patient outcomes among TB suspects screened by a single point-of-care Xpert MTB/RIF at a primary care clinic in Johannesburg, South Africa.**


Introduction: In December 2010, the World Health Organization recommended a single Xpert MTB/RIF assay as the initial diagnostic in people suspected of HIV-associated or drug resistant tuberculosis. Few data are available on the impact of this recommendation on patient outcomes. **We describe the diagnostic follow-up, clinical characteristics and outcomes of a cohort of tuberculosis suspects screened using a single point-of-care Xpert.**

Methods: **Consecutive tuberculosis suspects at a primary care clinic in Johannesburg, South Africa were assessed for tuberculosis using point-of-care Xpert.** Sputum smear microscopy and liquid culture were performed as reference standards. Xpert-negatives were evaluated clinically, and further assessed at the discretion of clinicians. Participants were followed for six months.
Results: From July-September 2011, 641 tuberculosis suspects were enrolled, of whom 69% were HIV-infected. Eight percent were positive by a single Xpert. Among 116 individuals diagnosed with TB, 66 (57%) were Xpert negative, of which 44 (67%) were empirical or radiological diagnoses and 22 (33%) were Xpert negative/culture-positive. The median time to tuberculosis treatment was 0 days (IQR: 0–0) for Xpert positives, 14 days (IQR: 5–35) for those diagnosed empirically, 14 days (IQR: 7–29) for radiological diagnoses, and 144 days (IQR: 28–180) for culture positives. Xpert negative tuberculosis cases were clinically similar to Xpert positives, including HIV status and CD4 count, and had similar treatment outcomes including mortality and time to antiretroviral treatment initiation.

Conclusions: In a high HIV-burden setting, a single Xpert identified less than half of those started on tuberculosis treatment, highlighting the complexity of TB diagnosis even in the Xpert era. Xpert at point-of-care resulted in same day treatment initiation in Xpert-positives, but had no impact on tuberculosis treatment outcomes or mortality.

Editor’s notes: This is one of the first reports of clinical outcomes for people with suspected TB undergoing investigation using Xpert MTB/RIF in routine clinical care in South Africa. The data are from a single primary health care clinic in Johannesburg which had an on-site Xpert instrument. 69% of the people with suspected TB also had HIV infection; among those, 45% were on ART at enrolment and the median CD4+ cell count was 276 cells/µl. The diagnostic performance of Xpert was similar to that previously reported with sensitivity of a single Xpert (compared to culture) of 66%. Only 8% of suspects were Xpert positive, but Xpert positives accounted for fewer than half of those started on TB treatment within two months, with many diagnoses still based on clinical and radiological grounds. Over three-quarters of Xpert positive cases were started on treatment on the same day as sputum collection which demonstrates the potential impact of point-of-care placement. The authors attempted to explore the impact of Xpert on treatment outcomes and mortality by comparing outcomes between Xpert-positive cases and Xpert-negative cases but this requires cautious interpretation since it is not a comparison between randomised groups. Overall mortality was very low (by 6 months, <1% in all people with suspected TB, and only 2% among people starting TB treatment), perhaps partly a reflection of the high proportion of people already taking ART and relatively high CD4+ cell counts. One concerning finding was a relatively high proportion of TB cases who started treatment but had defaulted before 6 months (23% vs. 12% for Xpert-positive vs. Xpert-negative cases), but there is no comparison with the 'usual' default rates at this clinic. Further studies reporting clinical outcomes of people investigated for TB using Xpert are awaited.

4. Close the resource gap

Combination HIV Prevention: The Value and Interpretation of Mathematical Models.


Mathematical models of HIV prevention interventions often provide critical insights related to programmatic design and economic efficiency. One recent dynamic model by Long et al. highlights that a combination prevention approach - with testing, treatment, circumcision, microbicides and PrEP - may decrease transmissions by over 60 % and may be very cost-effective in South Africa. In this analysis, the authors introduce the critical concept of joint effectiveness of preventions programs and demonstrate how some programs operate synergistically (HIV screening coupled with early treatment) while others may create redundancies (microbicides coupled with pre-exposure prophylaxis). Whether combination HIV prevention programs perform with additive, multiplicative or maximal effectiveness will be important to consider in anticipation of their combined transmission impact.
Editor’s notes: This commentary highlights important concepts and results from a recent modelling study of combination prevention for HIV in South Africa. A key concept discussed is that of ‘joint effectiveness’, which considers how two or more intervention programmes, might work together in the same population. While multiplicative effectiveness is often assumed, other options are to optimistically assume additive effectiveness, where distinct, non-interacting parts of the population use and benefit from the different interventions, or to conservatively assume maximal effectiveness, where it is the same individuals who use and/or benefit from all of the interventions, substantially reducing the overall impact. The commentary also highlights the synergies and redundancies found in the study between different intervention components, and illustrates how the discounting of future costs and benefits used in this and other cost-effectiveness studies can affect the relative cost-effectiveness of different interventions depending upon when costs are incurred and benefits accrued. These are all important considerations for future modelling and cost-effectiveness studies looking at combination HIV prevention.

5. Eliminate gender inequalities

The disproportionate high risk of HIV infection among the urban poor in sub-Saharan Africa.


The link between HIV infection and poverty in sub-Saharan Africa (SSA) is rather complex and findings from previous studies remain inconsistent. While some argue that poverty increases vulnerability, existing empirical evidence largely support the view that wealthier men and women have higher prevalence of HIV. In this paper, we examine the association between HIV infection and urban poverty in SSA, paying particular attention to differences in risk factors of HIV infection between the urban poor and non-poor. The study is based on secondary analysis of data from the Demographic and Health Surveys from 20 countries in SSA, conducted during 2003-2008. We apply multilevel logistic regression models, allowing the urban poverty risk factor to vary across countries to establish the extent to which the observed patterns are generalizable across countries in the SSA region. The results reveal that the urban poor in SSA have significantly higher odds of HIV infection than urban non-poor counterparts, despite poverty being associated with a significantly lower risk among rural residents. Furthermore, the gender disparity in HIV infection (i.e. the disproportionate higher risk among women) is amplified among the urban poor. The paper confirms that the public health consequence of urban poverty that has been well documented in previous studies with respect to maternal and child health outcomes does apply to the risk of HIV infection. The positive association between household wealth and HIV prevalence observed in previous studies largely reflects the situation in the rural areas where the majority of the SSA populations reside.

Abstract Full-text [free] access

Editor’s notes: Evidence on the association between socio-economic position and HIV incidence in sub-Saharan Africa (SSA) has been mixed and appears to be changing over time. Although wealth was previously a predictor of HIV infection, it has recently been suggested that poverty is increasingly driving new infections in mature epidemics, especially in rural areas, where the majority of the population in SSA resides. With high rates of urbanisation both in SSA and globally (according to UNAIDS 2 of every 3 people living with HIV will be living in urban areas by 2030), this article provides important disaggregated evidence of the higher risk of HIV infection among the urban poor as well, and particularly among poor urban women. Even after controlling for sexual behaviour, the results suggest that other structural factors that characterise the environment, in which the urban poor live, such as unemployment, discrimination and violence, may be playing a key role. Interestingly, higher educational attainment was found to be associated with higher HIV risk among the urban poor, while it appeared to be protective among the better-off urban population. This may be pointing towards the ‘inverse equity hypothesis’, discussed in another paper this month (Hargreaves et al.), whereby groups with higher socio-economic position (wealth and/or education) are
expected to benefit first from HIV/health interventions, thereby initially widening the gap in health outcomes until the poor catch up.

6. Eliminate stigma and discrimination

'The intention may not be cruel... but the impact may be': understanding legislators’ motives and wider public attitudes to a draft HIV Bill in Malawi.

Stackpool-Moore, L. Sexually Transmitted Infections. 2013. June 89 (4)

Objectives: The law in relation to HIV has prominence in the formation and regulation of moral norms-in regard to human rights, and in regard to criminalisation, the policing of sexuality and intimate behaviours, and the production of stigma. The research focuses on the potential and impotence of the law to govern for, and enable, the human right to health in the context of HIV in Malawi.

Methods: This one-country qualitative case study (Malawi) action research involved data collection during a 6-month period (October 2010-March 2011). Datasets include interviews with law commissioners (n=10), opinion leaders (n=22), life story participants who were people living with and closely affected by HIV (n=20), reflections of the action research team (n=6), and a review of the proposed HIV and AIDS (Prevention and Management) Bill, legal and policy documents.

Results: The analysis of the perspectives of the law commissioners, who formed the Special Law Commission and drafted the Bill, revealed that stigma was consciously invoked to delineate social norms and guide governance of notions of personal responsibility. The analysis of the perspectives of the life story participants, whose lives would be most directly impacted if these provisions came into force, reveals the extent to which the stigma associating criminality and HIV is falling on fertile ground through its engagement and generation of internalised stigma; unearthing an uneasy link between stigma and the law in response to HIV in Malawi.

Discussion: The results indicated that the proposed HIV Bill in Malawi manifests a tension between intention and impact. By incorporating criminal sanctions as part of the proposed HIV Bill, the lawmakers actively seek to use stigma to shape social attitudes and attempt to guide normative behaviour.

Abstract access

Editor’s notes: This paper presents research that examines the impact of criminal law in relation to HIV on stigma in Malawi. Through interviews with lawmakers and life story interviews with people living with and closely affected by HIV, the author examined how participants understand the proposed draft HIV and AIDS (Prevention and Management) Bill. The legal initiative for the bill, whilst based on principles of non-discrimination, includes provision to imprison a person who knows that he (sic) is HIV positive and does not refrain from an act which is likely to infect another person or who deliberately infects another person. Of great concern, the interviews revealed that whilst participants stated a support for non-discrimination of people living with HIV, many supported criminalisation of HIV transmission. The lawmakers were almost unanimously in favour of criminalising HIV transmission as a way to seek retribution and justice rather than for prevention of HIV transmission. The author noted that the lawmakers were particularly judgemental and moralistic about the issue. The people living with or affected by HIV were less certain and provided arguments for and against criminalisation, especially in relation to deliberate transmission of HIV where knowledge of status is not known. They were particularly worried that this law may dissuade people from testing. This paper provides an important understanding of the tension between political level intent to reduce stigma around HIV and the moralizing position taken by law- and policy makers. More worryingly, the author suggests that the perpetuation of stigma through such means as this law could be used to maintain or establish social control.
7. Eliminate travel restrictions

HIV-related travel restrictions: trends and country characteristics.


Introduction: Increasingly, HIV-seropositive individuals cross international borders. HIV-related restrictions on entry, stay, and residence imposed by countries have important consequences for this mobile population. Our aim was to describe the geographical distribution of countries with travel restrictions and to examine the trends and characteristics of countries with such restrictions.

Methods: In 2011, data presented to UNAIDS were used to establish a list of countries with and without HIV restrictions on entry, stay, and residence and to describe their geographical distribution. The following indicators were investigated to describe the country characteristics: population at mid-year, international migrants as a percentage of the population, Human Development Index, estimated HIV prevalence (age: 15–49), presence of a policy prohibiting HIV screening for general employment purposes, government and civil society responses to having non-discrimination laws/regulations which specify migrants/mobile populations, government and civil society responses to having laws/regulations/policies that present obstacles to effective HIV prevention, treatment, care, and support for migrants/mobile populations, Corruption Perception Index, and gross national income per capita.

Results: HIV-related restrictions exist in 45 out of 193 WHO countries (23%) in all regions of the world. We found that the Eastern Mediterranean and Western Pacific Regions have the highest proportions of countries with these restrictions. Our analyses showed that countries that have opted for restrictions have the following characteristics: smaller populations, higher proportions of migrants in the population, lower HIV prevalence rates, and lack of legislation protecting people living with HIV from screening for employment purposes, compared with countries without restrictions.

Conclusion: Countries with a high proportion of international migrants tend to have travel restrictions – a finding that is relevant to migrant populations and travel medicine providers alike. Despite international pressure to remove travel restrictions, many countries continue to implement these restrictions for HIV-positive individuals on entry and stay. Since 2010, the United States and China have engaged in high profile removals. This may be indicative of an increasing trend, facilitated by various factors, including international advocacy and the setting of a UNAIDS goal to halve the number of countries with restrictions by 2015.

Abstract Full-text [free] access

Editor’s notes: Travel restrictions for people living with HIV were adopted by many governments in the early years of the epidemic when little was known about the disease and when there was great fear regarding its spread. This study describes the situation of such restrictions as of 2011, and the geographical distribution of countries with restrictions. Restrictions were present in almost a quarter of WHO countries, with little change in the total of numbers in the past 20 years, despite high profile examples of the US and China removing travel restrictions. Health practitioners working with mobile populations are well placed to advise and educate individuals who may be affected by these restrictions. Impacts on individual health include an increased risk of interrupted adherence to ARV medication, risk of deportation and detainment, which may limit access to treatment, and risk of psychological stress in travel/immigration process.

8. Strengthening HIV integration

Integrated maternal and child health services in Mozambique: structural health system limitations overshadow its effect on follow-up of HIV-exposed infants.
Background: The follow-up of HIV-exposed infants remains a public health challenge in many Sub-Saharan countries. Just as integrated antenatal and maternity services have contributed to improved care for HIV-positive pregnant women, so too could integrated care for mother and infant after birth improve follow-up of HIV-exposed infants. We present results of a study testing the viability of such integrated care, and its effects on follow-up of HIV-exposed infants, in Tete Province, Mozambique.

Methods: Between April 2009 and September 2010, we conducted a mixed-method, intervention-control study in six rural public primary healthcare facilities, selected purposively for size and accessibility, with random allocation of three facilities each for intervention and control groups. The intervention consisted of a reorganization of services to provide one-stop, integrated care for mothers and their children under five years of age. We collected monthly routine facility statistics on prevention of mother-to-child HIV transmission (PMTCT), follow-up of HIV-exposed infants, and other mother and child health (MCH) activities for the six months before (January-June 2009) and 13 months after starting the intervention (July 2009-July 2010). Staff were interviewed at the start, after six months, and at the end of the study. Quantitative data were analysed using quasi-Poisson models for significant differences between the periods before and after intervention, between healthcare facilities in intervention and control groups, and for time trends. The coefficients for the effect of the period and the interaction effect of the intervention were calculated with their p-values. Thematic analysis of qualitative data was done manually.

Results: One-stop, integrated care for mother and child was feasible in all participating healthcare facilities, and staff evaluated this service organisation positively. We observed in both study groups an improvement in follow-up of HIV-exposed infants (registration, follow-up visits, serological testing), but frequent absenteeism of staff and irregular supply of consumables interfered with healthcare facility performance for both intervention and control groups.

Conclusions: Despite improvement in various aspects of the follow-up of HIV-exposed infants, we observed no improvement attributable to one-stop, integrated MCH care. Structural healthcare system limitations, such as staff absences and irregular supply of essential commodities, appear to overshadow its potential effects. Regular technical support and adequate basic working conditions are essential for improved performance in the follow-up of HIV-exposed infants in peripheral public healthcare facilities in Mozambique.

Abstract  Full-text [free] access

Editor’s notes: Despite rapid advances in the delivery of PMTCT services in many sub-Saharan African countries, the follow-up of HIV-exposed infants until the age of 18 months remains a critical challenge. This mixed methods, quasi-experimental evaluation study evaluated the viability of providing one-stop, integrated care, its acceptability to healthcare providers, and its effect upon the follow-up of HIV-exposed infants and other MCH services, in the public health system. The intervention consisted of a reorganization of MCH services, to deliver integrated, one-stop consultations for mothers and their children up to 5 years of age. Absence of MCH staff occurred in 16% of months, and stock-outs of HIV testing commodities and MCH drugs occurred in almost half of all months. The improvements in both arms suggests that improving some of the basic working conditions of peripheral MCH staff and ensuring an adequate supply of commodities might be effective ways to improve the follow-up of HIV-exposed infants in peripheral public healthcare facilities in Mozambique.