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UNAIDS
1. Reduce sexual transmission

Emerging themes for sensitivity training modules of African healthcare workers attending to men who have sex with men: a systematic review.


Sensitivity training of front-line African health care workers (HCWs) attending to men who have sex with men (MSM) is actively promoted through national HIV prevention programming in Kenya. Over 970 Kenyan-based HCWs have completed an eight-modular online training free of charge (http://www.marps-africa.org) since its creation in 2011. Before updating these modules, we performed a systematic review of published literature of MSM studies conducted in sub-Saharan Africa (sSA) in the period 2011-2014, to investigate if recent studies provided: important new knowledge currently not addressed in existing online modules; contested information of existing module topics; or added depth to topics covered already. We used learning objectives of the eight existing modules to categorise data from the literature. If data could not be categorised, new modules were suggested. Our review identified 142 MSM studies with data from sSA, including 34 studies requiring module updates, one study contesting current content, and 107 studies reinforcing existing module content. ART adherence and community engagement were identified as new modules. Recent MSM studies conducted in sSA provided new knowledge, contested existing information, and identified new areas of MSM service needs currently unaddressed in the online training.

Abstract Full-text [free] access

Editor’s notes: Same sex practices remain criminalised in sub-Saharan Africa. Gay men and other men who have sex with men face stigma, discrimination, harassment and arrest. Health care workers frequently have no training on issues affecting gay men and other men who have sex with men and are ill-prepared to work sensitively with them. Together these can deter these men from accessing health care and HIV/STI services, increasing their risk of HIV and other poor health outcomes.

This study conducted a systematic review of gay men and other men who have sex with men in sub-Saharan Africa. The findings were used to update an on-line training programme for health care workers in Kenya. This previously comprised modules on i) men who have sex with men and HIV in Africa ii) homophobia: stigma and its effects; iii) sexual identity, coming out and disclosure; iv) anal sex and common sexual practices; v) HIV and STIs; vi) condom and lubricant use; vii) mental health: anxiety, depression and substance use; and viii) risk-reduction counselling. The review updated the training programme with new evidence and two new modules were introduced: ix) ART adherence; and x) community engagement.

Health care workers play a crucial role in reducing stigma and discrimination facing gay men and other men who have sex with men. This systematic review provided a valuable step in updating an important, accessible training programme. Reducing homoprejudice and ensuring health care workers have accurate and up-to-date knowledge are key to improving service uptake by gay men and other men who have sex with men.

Impact of nucleic acid testing relative to antigen/antibody combination immunoassay on the detection of acute HIV infection.

Objective: To assess the addition of HIV nucleic acid testing (NAT) to fourth-generation (4thG) HIV antigen/antibody combination immunoassay in improving detection of acute HIV infection (AHI).

Methods: Participants attending a major voluntary counseling and testing site in Thailand were screened for AHI using 4thG HIV antigen/antibody immunoassay and sequential less sensitive HIV antibody immunoassay. Samples nonreactive by 4thG antigen/antibody immunoassay were further screened using pooled NAT to identify additional AHI. HIV infection status was verified following enrollment into an AHI study with follow-up visits and additional diagnostic tests.

Results: Among 74,334 clients screened for HIV infection, HIV prevalence was 10.9% and the overall incidence of AHI (N = 112) was 2.2 per 100 person-years. The inclusion of pooled NAT in the testing algorithm increased the number of acutely infected patients detected, from 81 to 112 (38%), relative to 4thG HIV antigen/antibody immunoassay. Follow-up testing within 5 days of screening marginally improved the 4thG immunoassay detection rate (26%). The median CD4 T-cell count at the enrollment visit was 353 cells/µL and HIV plasma viral load was 598 289 copies/ml.

Conclusion: The incorporation of pooled NAT into the HIV testing algorithm in high-risk populations may be beneficial in the long term. The addition of pooled NAT testing resulted in an increase in screening costs of 22% to identify AHI: from $8.33 per screened patient to $10.16. Risk factors of the testing population should be considered prior to NAT implementation given the additional testing complexity and costs.

Abstract access

Editor’s notes: Acute HIV infection (AHI) is generally defined as the time between HIV acquisition and the appearance of detectable antibodies. Individuals with AHI are highly infectious, at least partly due to high viral load. Effective strategies to identify people with AHI could therefore plausibly reduce transmission, although the extent to which AHI drives transmission at a population level continues to be debated. Although the fourth generation immunoassays, incorporating detection of p24 antigen, have been shown to detect infection earlier, there is still a period during which only HIV ribonucleic acid (RNA) can be detected. High costs limit the routine use of HIV RNA testing for this purpose. Pooling samples is one way to potentially reduce costs.

This research was part of a study aimed at detection and treatment of AHI in an urban population of predominantly gay men and other men who have sex with men in Bangkok. Samples that tested negative on fourth generation immunoassay were pooled (median pool size was 14 samples) before undergoing HIV RNA testing. Some 31 pools were positive (0.5% of pools tested) and one positive specimen was then identified from each of those pools. Overall, this constituted only around a quarter of all AHI cases detected. The remainder were defined as AHI on the basis of positive fourth generation but negative second and third generation antibody tests. Individuals detected only by HIV RNA had somewhat lower viral loads than people detected by immunoassay. Follow-up testing illustrated that this was a time when viral load was increasing rapidly. This highlights the potential impact that detection and treatment at this stage could have on reducing onward transmission.

Although interpretation of the study is somewhat complicated by the use of several different assays during the study and complicated algorithms to define outcomes, the basic message seems clear. Fourth generation immunoassays may detect the majority of acute infections. But there may still be a
role for pooled HIV RNA testing in certain key populations to maximize detection of AHI. This study was not really designed to evaluate the real world impact of the testing strategy, as follow-up was very tightly controlled and almost all people initiated ART within one week. Although there was some basic costing analysis included, more detailed cost-effectiveness studies will be important to understand whether or not pooled HIV RNA testing has a role in routine practice.

Implementation and operational research: evaluation of loss-to-follow-up and postoperative adverse events in a voluntary medical male circumcision program in Nyanza Province, Kenya.


Background: More than 4.7 million voluntary medical male circumcisions (VMMCs) had been provided by HIV prevention programs in sub-Saharan Africa through 2013. All VMMC clients are recommended to return to the clinic for postoperative follow-up, although adherence is variable. The clinical status of clients who do not return is largely unknown.

Methods: VMMC clients from Nyanza Province, Kenya, aged older than or equal to 13 years, were recruited immediately after surgery from April to October 2012 from high-volume sites. Medical record reviews at 13-14 days after surgery indicated which clients had been adherent with recommended follow-up (ADFU) and which were lost-to-follow-up (LTFU). Clients in the LTFU group received clinical evaluations at home approximately 2 weeks postsurgery. Adverse events (AEs) and AE rates were compared between the ADFU and LTFU groups.

Results: Of 4504 males approached in 50 VMMC sites, 1699 (37.7%) were eligible and enrolled and 1600 of 1699 (94.2%) contributed to follow-up and AE data. Medical record review indicated 897 of 1600 (56.1%) were LTFU, and 762 (84.9%) of these received home-based clinical evaluations. The rate of moderate or severe AE diagnosis was 6.8% in the LTFU group vs. 3.3% in the ADFU group (relative risk = 2.1, 95% confidence interval: 1.3 to 3.4).

Conclusions: The moderate or severe AE diagnosis rate was approximately 2 times higher in the LTFU group. National programs should consider instituting surveillance systems to detect AEs that might otherwise go unnoticed. Providers should emphasize the importance of follow-up and actively contact LTFU clients to ensure care is provided throughout the entire postoperative course for all.

Abstract access

Editor’s notes: Latest estimates suggest that over nine million men have undergone voluntary medical male circumcision (VMMC) to reduce their risk of HIV infection. In Kenya, VMMC clients are instructed to return to the clinic site within seven days of surgery for follow-up including assessment of adverse events (AEs). In this large study, over half of circumcised men from 50 sites did not return to the clinic for follow-up. These men were more likely to be 18 to 24 years (versus younger or older than this), with little formal education, without access to a car, and using multiple transportation methods. Follow-up of these men at home indicated that they had over twice the risk of a moderate or severe AE compared with individuals who did adhere to recommended follow-up (ADFU). The difference in risk between the ADFU and LTFU groups was mainly for infection, wound disruption and pain. The study confirms that VMMC clients who do not return to the clinic should not be assumed to be healing without complications, and VMMC programmes should try novel approaches to improve follow-up rates and continue to reinforce the importance of follow-up.
We sought to describe the advantage of rapid tests over ELISA tests in community-based screening for HIV among men who have sex with men (MSM) in urban areas of China. Data of 31,406 screening tests conducted over six months in 2011 among MSM across 12 areas were analyzed to compare the differences between those receiving rapid testing and ELISA. Rapid tests accounted for 45.8% of these screening tests. The rate of being screened positive was 7.2% among rapid tests and 5.3% for ELISA tests ($\chi^2 = 49.161, p < 0.001$). This advantage of rapid test in HIV case finding persisted even when socio-demographic, behavioural, screening recruitment channel and city were controlled for in logistic regression ($\exp[\beta] = 1.42, p < 0.001, 95\% \text{ CI} = 1.27,1.59$). MSM who received rapid tests, compared with those tested by ELISA, were less likely to use condoms during last anal sex (50.8% vs. 72.3%, $\chi^2 = 1706.146, p < 0.001$), more likely to have multiple sex partners (55.7% vs. 49.5%, $\chi^2 = 238.188, p < 0.001$) and less likely to have previously undergone HIV testing (38.8% vs. 54.7%, $\chi^2 = 798.476, p < 0.001$). These results demonstrate the robustness of the advantage of rapid tests over traditional ELISA tests in screening for MSM with HIV infection in cooperation with community-based organizations in urban settings in China.
value (PPV) of four adherence measures. We also assessed factors associated with misreporting of adherence using multiple drug-concentration thresholds and explored pill use and misreporting using semi-structured interviews (SSIs). Reporting use of ≥1 pill in the previous 7 days had the highest PPV, while pill-count data consistent with missing ≤1 day had the lowest PPV. However, all four measures demonstrated poor PPV. Reported use of oral contraceptives (OR 2.26; p = 0.014) and weeks of time in the study (OR 1.02; p < 0.001) were significantly associated with misreporting adherence. Although most SSI participants said they did not misreport adherence, participant-dependent adherence measures were clearly unreliable in the FEM-PrEP trial. Pharmacokinetic monitoring remains the measure of choice until more reliable participant-dependent measures are developed.

Abstract

Editor’s notes: A number of studies have demonstrated that pre-exposure prophylaxis (PrEP) is effective in reducing HIV transmission when adherence is high. Understanding factors affecting adherence, and evaluating methods to best measure adherence are therefore of crucial importance. Despite excellent self-reported adherence, the FEM-PrEP and VOICE trials did not illustrate a benefit of PrEP. In this study, drug concentrations were assessed in 1200 visits from 150 FEM-PrEP trial participants to determine adherence. These results were used to assess the accuracy of three measures of self-reported adherence and also pill counting. All four measures had poor positive predictive value, ranging from 26.2% to 42.4%. There was an increase in misreporting of adherence over time which may be associated with lower adherence levels over time. In semi-structured interviews, most participants said that they did not misreport adherence. The authors call for improvements in methods to reduce socially desirable responses through participant self-report, and examination of the reasons why people join HIV prevention trials. Future trials may also need to consider using drug concentrations in addition to currently used methods to better estimate adherence.

Repeat use of post-exposure prophylaxis for HIV among Nairobi-based female sex workers following sexual exposure.


As ART-based prevention becomes available, effectively targeting these interventions to key populations such as female sex workers (FSW) will be critical. In this study we analyze patterns of repeated post-exposure prophylaxis (PEP) access in the context of a large FSW program in Nairobi. During close to 6000 person-years of follow-up, 20% of participants (n = 1119) requested PEP at least once and 3.7% requested PEP more than once. Repeat PEP users were younger, had a higher casual partner volume, and were more likely to use condoms with casual and regular partners, have a regular partner, and test for HIV prior to enrolment. Barriers to PEP included stigma, side effects, and lack of knowledge, suggesting repeated promotion may be required for higher rates of uptake. A small subset of FSW, potentially those with heightened risk perception, showed a higher frequency of PEP use; these individuals may be most amenable to rollout of pre-exposure prophylaxis.

Abstract access

Editor’s notes: Antiretroviral therapy based HIV prevention is growing, particularly the use of Pre-exposure prophylaxis (PrEP) which is effective when adherence is high. However, given the
challenges associated with adherence, other options are essential. Post-exposure prophylaxis (PEP) following sexual exposure to HIV is an HIV prevention strategy that could be of benefit in some situations, and is recommended for risky exposure settings. This paper describes PEP use among sex workers in Nairobi. In particular, this paper examined repeat PEP use and the characteristics of female sex workers returning for additional courses of PEP. Interestingly, repeat PEP users seemed to perceive that they were at increased risk of HIV and were also more aware of PEP as a prevention option. Individuals who did not use PEP knew little to nothing about it, were afraid of stigma from community members and health care providers, and were concerned about side effects which they knew about from people on HIV treatment. These are essential factors to take into account when developing an implementation programme for future programmes, and especially PrEP which can learn from the past but will undoubtedly forge new paths in HIV prevention implementation and programming.

2. Prevent HIV among drug users

The impact of adherence to preexposure prophylaxis on the risk of HIV infection among people who inject drugs.


Objective: To describe participant adherence to daily oral tenofovir in an HIV preexposure prophylaxis (PrEP) trial, examine factors associated with adherence, and assess the impact of adherence on the risk of HIV infection.

Design: The Bangkok Tenofovir Study was a randomized, double-blind, placebo-controlled trial conducted among people who inject drugs, 2005-2012.

Methods: Participants chose daily visits or monthly visits. Study nurses observed participants swallow study drug and both initialed a diary. We assessed adherence using the diary. We examined adherence by age group and sex and used logistic regression to evaluate demographics and risk behaviors as predictors of adherence and Cox regression to assess the impact of adherence on the risk of HIV infection.

Results: A total of 2413 people enrolled and contributed 9665 person-years of follow-up (mean 4.0 years, maximum 6.9 years). The risk of HIV infection decreased as adherence improved, from 48.9% overall to 83.5% for those with at least 97.5% adherence*. In multivariable analysis, men were less adherent than women (P = 0.006) and participants 20-29 years old (P < 0.001) and 30-39 years old (P = 0.01) were less adherent than older participants. Other factors associated with poor adherence included incarceration (P = 0.02) and injecting methamphetamine (P = 0.04).

Conclusion: In this HIV PrEP trial among people who inject drugs, improved adherence to daily tenofovir was associated with a lower risk of HIV infection. This is consistent with trials among MSM and HIV-discordant heterosexual couples and suggests that HIV PrEP can provide a high level of protection from HIV infection.

*The authors mean that effectiveness improved from 48.9% overall to 83.5% in those who were 97.5% adherent.

Abstract access
**Editor’s notes:** Randomised controlled trials have illustrated that daily oral tenofovir as pre-exposure prophylaxis (PrEP) can reduce HIV transmission. In this study, using data from the only PrEP trial to be completed among people who inject drugs, the investigators assessed the impact of directly-observed adherence to PrEP on the incidence of HIV infection in the Bangkok Tenofovir Study. Adherence was defined as the proportion of days recorded in the participants’ diaries that the participant took the study drug. On average, participants took the study drug on 84% of days. Their findings of a strong association of increasing levels of adherence with reduced risk of HIV infection add to existing literature on the importance of adherence for PrEP effectiveness among gay men and other men who have sex with men and HIV-discordant couples. The novelty of this study was to directly observe adherence to PrEP. Directly observed ART treatment has been used in prisons and drug treatment centres, and the potential of this method to improve adherence estimation is interesting.

3. **Eliminate new HIV infections among children**

**Prevention of mother-to-child transmission of syphilis and HIV in China: What drives political prioritization and what can this tell us about promoting dual elimination?**


**Objective:** The present study aims to identify reasons behind the lower political priority of mother-to-child transmission (MTCT) of syphilis compared with HIV, despite the former presenting a much larger and growing burden than the latter, in China, over the 20 years prior to 2010.

**Methods:** We undertook a comparative policy analysis, based on informant interviews and documentation review of control of MTCT of syphilis and HIV, as well as nonparticipant observation of relevant meetings/trainings to investigate agenda-setting prior to 2010.

**Results:** We identified several factors contributing to the lower priority accorded to MTCT of syphilis: relative neglect at a global level, dearth of international financial and technical support, poorly unified national policy community with weak accountability mechanisms, insufficient understanding of the epidemic and policy options, and a prevailing negative framing of syphilis that resulted in significant stigmatization.

**Conclusion:** A dual elimination goal will only be reached when prioritization of MTCT of syphilis is enhanced in both the international and national agendas.
equality agenda, and the recent severe acute respiratory syndrome (SARS) outbreak had further underscored the importance of controlling infectious diseases. Alongside this, the national ‘blood selling’ scandal, during which hundreds of thousands of rural Chinese acquired HIV through blood selling in the 90s, was receiving increasing attention in international media. This contributed to a different framing of the HIV issue, away from the stigmatising ‘immoral’ narrative to an ‘innocent victims’ narrative. Congenital syphilis, unfortunately, continued to suffer from a stigmatising framing. However, delivery platforms for the effective prevention of mother-to-child transmission of HIV have been established and could be used for a dual control and elimination approach, with greater health benefits. The authors conclude that greater policy prioritisation could be achieved with a more nuanced framing of the two infections as being linked when it comes to underlying vulnerability and feasibility of solutions. It will require a strong partnership and collaboration between the mother-to-child transmission of syphilis and HIV policy communities.

Effect of cytomegalovirus infection on breastfeeding transmission of HIV and on the health of infants born to HIV-infected mothers.


Background: Cytomegalovirus (CMV) infection can be acquired in utero or postnatally through horizontal transmission and breastfeeding. The effect of postnatal CMV infection on postnatal HIV transmission is unknown.

Methods: The Breastfeeding, Antiretrovirals and Nutrition study, conducted in Malawi, randomized 2369 mothers and their infants to three antiretroviral prophylaxis arms - mother (triple regimen), infant (nevirapine), or neither - for 28 weeks of breastfeeding, followed by weaning. Stored plasma and peripheral blood mononuclear cell specimens were available for 492 infants at 24 weeks and were tested with CMV PCR. Available samples from infants who were CMV PCR-positive at 24 weeks were also tested at birth (N = 242), and from infants PCR-negative at 24 weeks were tested at 48 weeks (N = 96). Cox proportional-hazards models were used to determine if CMV infection was associated with infant morbidity, mortality, or postnatal HIV acquisition.

Results: At 24 weeks of age, CMV DNA was detected in 345/492 infants (70.1%); the estimated congenital CMV infection rate was 2.3%, and the estimated rate of CMV infection at 48 weeks was 78.5%. CMV infection at 24 weeks was associated with subsequent HIV acquisition through breastfeeding or infant death between 24 and 48 weeks of age (hazard ratio 4.27, P = 0.05).

Conclusion: Most breastfed infants of HIV-infected mothers in this resource-limited setting are infected with CMV by 24 weeks of age. Early CMV infection may be a risk factor for subsequent infant HIV infection through breastfeeding, pointing to the need for comprehensive approaches in order to achieve elimination of breastfeeding transmission of HIV.

Abstract access

Editor’s notes: Studies have illustrated that mother-to-child HIV transmission is more frequent among neonates with congenital cytomegalovirus (CMV) infection. Infants co-infected with HIV and CMV have higher rates of HIV disease progression and death. This study using data and samples of infant plasma and peripheral blood mononuclear cells are from the Breastfeeding, Antiretrovirals and Nutrition (BAN) randomised, controlled clinical trial (RCT). The study examines whether postnatal
CMV infection in the infant is associated with HIV transmission through breastfeeding. The study investigates the relationship between postnatal antiretroviral therapy and postnatal CMV acquisition. The data suggests that early postnatal CMV infection in an HIV-exposed uninfected infant may predict subsequent HIV transmission through breastfeeding and infant mortality. The study confirmed previous findings that approximately 70% of breastfed infants born to mothers living with HIV in low-income settings acquire CMV infection by six months of age. However, the study did not find an association between maternal antiretroviral therapy and the risk of postnatal CMV transmission. It is important to note that in the RCT, antiretroviral therapy was only initiated at the onset of labour. The effect of maternal antiretroviral therapy taken earlier in pregnancy on the prevention or delay of CMV acquisition remains unknown, although a few observational studies have found that maternal antiretroviral therapy reduces congenital and early postnatal CMV infection. It is biologically plausible that antiretroviral therapy reduces or prevents CMV reactivation in the mother, thus preventing transient episodes of maternal CMV viraemia. This mechanism could explain reduced CMV transmission to the infant (be that before or after birth). HIV-exposed but uninfected infants experience higher morbidity and mortality; any such disease attributable to CMV could therefore potentially be reduced by initiation of antiretroviral therapy earlier in pregnancy.

HIV testing among pregnant women who attend antenatal care in Malawi.


Malawi adopted the Option B+ strategy in 2011. Its success in reducing MTCT depends on coverage and timing of HIV testing. We assessed HIV status ascertainment and its predictors during pregnancy. HIV status ascertainment was 82.3% (95%-CI 80.2-85.9) in the pre-Option B+ period and 85.7% (95%-CI 83.4-88.0) in the Option B+ period. Higher HIV ascertainment was independently associated with higher age, attending ANC more than once, and registration in 2010. The observed high variability of HIV ascertainment between sites (50.6%-97.7%) and over time suggests that HIV test kits shortages and insufficient numbers of staff posed major barriers to reducing MTCT.

Abstract access

Editor’s notes: UNAIDS has called for an end to mother-to-child HIV transmission through the Global Plan towards the elimination of new infections among children and keeping their mothers alive. WHO guidelines on the use of antiretroviral medicines for treating and preventing HIV infection in 2013 recommends two options for pregnant and breastfeeding women. One of which is lifelong antiretroviral therapy (ART) for all pregnant women living with HIV regardless of CD4 count or disease stage, commonly referred to as Option B+. The Global Plan requires that 90% of all women living with HIV have access to ART. The success of the Global Plan will depend on sufficient numbers of women being tested for HIV.

This study includes data from 19 secondary and primary health facilities offering antenatal care in Malawi, the first country to introduce the Option B+ strategy in 2011. Introduction of the Option B+ strategy did not result in a significant change in the proportion of women who underwent HIV testing. HIV ascertainment varied widely across facilities from 50% to 98%, and fluctuated greatly within sites over short time periods. The observed sudden decreases in numbers of women who received an HIV test suggest that important barriers to HIV testing exist at facility level. Previous studies have illustrated that temporary shortages of HIV testing kits and staff interrupt regular antenatal (ANC) HIV testing in health facilities. Women who had multiple ANC visits were more likely to have had their
HIV status ascertained, likely because multiple visits increased their chance to attend when staff and kits were available. Unfortunately, this study was unable to determine individual-level factors associated with HIV testing not having occurred.

We now have highly effective programmes that can virtually eliminate new HIV infections among children globally. To attain this goal, urgent attention must be paid to strengthening health systems. Elimination of new infections among children will require attention to the whole cascade of care from diagnosis of HIV, through to provision of results and treatment and supporting women to take ART consistently.

4. Avoid TB deaths

The impact of implementation fidelity on mortality under a CD4-stratified timing strategy for antiretroviral therapy in patients with tuberculosis.


Among patients with tuberculosis and human immunodeficiency virus type 1, CD4-stratified initiation of antiretroviral therapy (ART) is recommended, with earlier ART in those with low CD4 counts. However, the impact of implementation fidelity to this recommendation is unknown. We examined a prospective cohort study of 395 adult patients diagnosed with tuberculosis and human immunodeficiency virus between August 2007 and November 2009 in Kinshasa, Democratic Republic of the Congo. ART was to be initiated after 1 month of tuberculosis treatment at a CD4 count of <100 cells/mm$^3$ or World Health Organization stage 4 (other than extrapulmonary tuberculosis) and after 2 months of tuberculosis treatment at a CD4 count of 100-350 cells/mm$^3$. We used the parametric g-formula to estimate the impact of implementation fidelity on 6-month mortality. Observed implementation fidelity was low (46%); 54% of patients either experienced delays in ART initiation or did not initiate ART, which could be avoided under perfect implementation fidelity. The observed mortality risk was 12.0% (95% confidence interval (CI): 8.2, 15.7); under complete (counterfactual) implementation fidelity, the mortality risk was 7.8% (95% CI: 2.4, 12.3), corresponding to a risk reduction of 4.2% (95% CI: 0.3, 8.1) and a preventable fraction of 35.1% (95% CI: 2.9, 67.9). Strategies to achieve high implementation fidelity to CD4-stratified ART timing are needed to maximize survival benefit.

Abstract access

Editor’s notes: There is clear evidence from randomised controlled trials that the early initiation of antiretroviral therapy (ART) during TB treatment reduces mortality in HIV/TB co-infected people. That evidence has translated to policy and most countries now follow WHO guidelines which recommend treatment within eight weeks of starting TB treatment, and within two weeks in people with the most advanced immunodeficiency (CD4+ T-cell count <50cells/µL).

This paper presents a post hoc analysis from an intervention study evaluating integrated, nurse-delivered TB/HIV care in primary health care clinics in the Democratic Republic of the Congo. The parent study illustrated that integrated care led to better uptake of ART and lower mortality, in comparison to a historical cohort prior to integration. However, mortality was still substantial - around one in 10 participants died within six months - and under half of all participants failed to start ART on time. The definition of fidelity was quite tight, only five days allowed beyond the one-month or two-month timing threshold.
Analysis suggested that around a third of the mortality could have been prevented if ART had been started within the defined time periods. As in most studies, mortality was strongly associated with low CD4+ T-cell count (<50 cells/µL) and this group were responsible for much of what was considered to be unavoidable mortality. Additional strategies are clearly necessary to improve outcomes in this group alongside broader strategies to promote earlier diagnosis of HIV and TB.

5. Close the resource gap

Household illness, poverty and physical and emotional child abuse victimisation: findings from South Africa’s first prospective cohort study.


Background: Physical and emotional abuse of children is a large scale problem in South Africa, with severe negative outcomes for survivors. Although chronic household illness has shown to be a predictor for physical and emotional abuse, no research has thus far investigated the different pathways from household chronic illness to child abuse victimisation in South Africa.

Methods: Confidential self-report questionnaires using internationally utilised measures were completed by children aged 10-17 (n = 3515, 56.7% female) using door-to-door sampling in randomly selected areas in rural and urban locations of South Africa. Follow-up surveys were conducted a year later (96.7% retention rate). Using multiple mediation analyses, this study investigated direct and indirect effects of chronic household illness (AIDS or other illness) on frequent (monthly) physical and emotional abuse victimisation with poverty and extent of the ill person’s disability as hypothesised mediators.

Results: For children in AIDS-ill families, a positive direct effect on physical abuse was obtained. In addition, positive indirect effects through poverty and disability were established. For boys, a positive direct effect and indirect effect of AIDS-illness on emotional abuse through poverty were detected. For girls, a positive indirect effect through poverty was observed. For children in households with other chronic illness, a negative indirect effect on physical abuse was obtained. In addition, a negative indirect effect through poverty and positive indirect effect through disability was established. For boys, positive and negative indirect effects through poverty and disability were found respectively. For girls, a negative indirect effect through poverty was observed.

Conclusions: These results indicate that children in families affected by AIDS-illness are at higher risk of child abuse victimisation, and this risk is mediated by higher levels of poverty and disability. Children affected by other chronic illness are at lower risk for abuse victimisation unless they are subject to higher levels of household disability. Interventions aiming to reduce poverty and increase family support may help prevent child abuse in families experiencing illness in South Africa.

Abstract Full-text [free] access

Editor’s notes: Research has illustrated that children in an HIV-affected household in sub-Saharan Africa are at an increased risk of child maltreatment. This is the first longitudinal study to examine pathways from household chronic illness to child abuse in the developing world through multiple mediation analysis. Using confidential self-report questionnaires the study collected data from 3515 children (aged 10 to 17 years) in South Africa.
What is striking in their findings is the difference that they found in the relationship between risk of child abuse and the type of illness affecting the household, mediated by poverty and disability. They noted higher levels of physical and emotional abuse among HIV-affected households compared to households without HIV. However, they also found that households affected by other chronic illness had lower abuse prevalence rates. Given that diabetes and high blood pressure are more likely to affect older age people, the authors hypothesise that the ill member of the household would likely have access to a state pension and thus benefit from some protection from the risk of poverty. The exception to this hypothesis were households within this group who had high levels of disability.

This study provides a valuable contribution because previous research has primarily focused on AIDS or cancer-affected households. These households are likely to need to manage higher levels of associated stigma, a shorter perceived life expectancy and more complex treatment options. As such previous research may have presented a more extreme relationship between illness status of household and a child’s risk of abuse. The findings highlight the significance for activities and programming in identifying two groups of households which are at heightened risk for child abuse: HIV affected households; and households affected by other chronic conditions.

Expenditure analysis of HIV testing and counseling services using the cascade framework in Vietnam.


Objectives: Currently, HIV testing and counseling (HTC) services in Vietnam are primarily funded by international sources. However, international funders are now planning to withdraw their support and the Government of Vietnam (GVN) is seeking to identify domestic funding and generate client fees to continue services. A clear understanding of the cost to sustain current HTC services is becoming increasingly important to facilitate planning that can lead to making HTC and other HIV services more affordable and sustainable in Vietnam. The objectives of this analysis were to provide a snapshot of current program costs to achieve key program outcomes including 1) testing and identifying PLHIV unaware of their HIV status and 2) successfully enrolling HIV (+) clients in care.

Methods: We reviewed expenditure data reported by 34 HTC sites in nine Vietnamese provinces over a one-year period from October 2012 to September 2013. Data on program outcomes were extracted from the HTC database of 42,390 client records. Analysis was carried out from the service providers’ perspective.

Results: The mean expenditure for a single client provided HTC services (testing, receiving results and referral for care/treatment) was US $7.6. The unit expenditure per PLHIV identified through these services varied widely from US $22.8 to $741.5 (median: $131.8). Excluding repeat tests, the range for expenditure to newly diagnose a PLHIV was even wider (from US $30.8 to $1483.0). The mean expenditure for one successfully referred HIV client to care services was US $466.6. Personnel costs contributed most to the total cost.

Conclusions: Our analysis found a wide range of expenditures by site for achieving the same outcomes. Re-designing systems to provide services at the lowest feasible cost is essential to making HIV services more affordable and treatment for prevention programs feasible in Vietnam. The analysis also found that understanding the determinants and reasons for variance in service costs by site is an important enhancement to the cascade of HIV services framework now adapted for and extensively used in Vietnam for planning and evaluation.
Editor’s notes: Some 91% of expenditure for HIV testing and counselling (HTC) in Viet Nam is funded by international donors. As donors start to reduce their contributions in the coming years, more of the costs will have to be fronted by the government of Viet Nam. Consequently, this paper looks at the cost around diagnosing HIV within the context of the care and treatment cascade, including not only the cost per person diagnosed, but also the cost of successfully enrolling people who have tested positive for HIV into care and treatment. This is particularly important in the context of Viet Nam, where only 29% of people estimated to be living with HIV have ever been enrolled in care and treatment services.

An important finding of the paper is in the break-down of costs by input by facilities. The authors found that the cost of personnel account for 40% of total costs. More importantly, they also found that the personnel costs vary widely between facilities, which may suggest that some facilities are over-staffed and are not allocating tasks efficiently. This is a key finding. As financial resources become scarcer, savings may need to be found by determining the optimal level of staffing and task-shifting.

The paper illustrates, as is to be expected, that the cost per person successfully enrolled in care and treatment is substantially higher than the costs per person tested and per person testing positive. However, it is not entirely clear whether the extra cost is explained simply by the fact that the overhead and start-up costs are allocated to a smaller number of people, or whether there are additional costs involved in a successful referral. This area needs further exploration. Additionally, an interesting follow-up to this paper could take on the costing from a societal perspective with the aim to understand the relation between patient-level costs and the successful link between testing and referral to care and treatment services.

Cost per patient of treatment for rifampicin-resistant tuberculosis in a community-based program in Khayelitsha, South Africa.


Objectives: The high cost of rifampicin-resistant tuberculosis (RR-TB) treatment hinders treatment access. South Africa has a high RR-TB burden, and national policy outlines decentralisation to improve access and reduce costs. We analysed health system costs associated with RR-TB treatment by drug-resistance profile and treatment outcome in a decentralised programme.

Methods: Retrospective, routinely collected patient-level data were combined with unit cost data to determine costs for each patient in a cohort treated between January 2009 and December 2011. Drug costs were based on recommended regimens according to drug-resistance and treatment duration. Hospitalisation costs were estimated based on admission/discharge dates, while clinic visit and diagnostic/monitoring costs were estimated according to recommendations and treatment duration. Missing data were imputed.

Results: Among 467 patients (72% HIV-infected), 49% were successfully treated. Treatment was initiated in primary care for 62%, with the remainder as inpatients. The mean cost per patient treated was $7916 (range 260-87 140); ranging from $5369 among patients who did not complete treatment to $23 006 for treatment failure. Mean cost for successful treatment was $8359 (2585-32 506). Second-line drug resistance was associated with a mean cost of $15 567
versus $6852 for only first-line resistance, with the major cost difference due to hospitalisation. Costs reported in 2013 USD.

Conclusions: **RR-TB treatment cost was high, and varied according to treatment outcome.** Despite decentralisation, hospitalisation remained a significant cost, particularly among those with more extensive resistance and those with treatment failure. These cost estimates can be used to model the impact of new interventions to improve patient outcomes.

Abstract  Full-text [free] access

**Editor’s notes:** Prior to 2011, South African guidelines recommended all multidrug-resistant tuberculosis (MDR-TB) patients be hospitalized for at least six months, or until culture conversion. This policy was changed in 2011 to allow for decentralized ambulatory care for sputum smear-negative patients. This paper evaluates the cost of treating rifampicin-resistant TB in Khayelitsha, South Africa using patient-level data in order to accurately represent real-world patient pathways under the new policy.

The authors find that the cost of TB treatment under this new policy varies substantially according to drug resistance profile and treatment outcomes. Treatment was successful only in about half of the sample in this study. Treatment failed for roughly 20% (including ‘treatment failure’ and ‘death’ outcomes), and about 30% of people were lost from treatment. People for whom treatment failed were the most costly, at a mean cost of $23,006. These people were more often admitted to hospital during treatment, and had a longer average length of stay in hospital. People infected with TB strains which were defined as pre-extensively drug resistant or extensively drug resistant (XDR) were more likely to experience treatment failure. As a result they incurred a much higher cost than individuals with rifampicin mono-resistance or MDR-TB. People treated successfully incurred a mean cost of $8,359. This is substantially lower than the mean cost of $17,164 under previous treatment guidelines. These findings indicate that the new policy is less costly overall than the policy of hospitalization for all MDR-TB patients. However, costs still vary substantially according to drug resistance and treatment outcomes. In order to see further reduction of costs and improvement of cost-effectiveness, therefore, treatment failure must be further reduced.

**Effects of cash transfers on children’s health and social protection in sub-Saharan Africa: differences in outcomes based on orphan status and household assets.**


**Background:** Unconditional and conditional cash transfer programmes (UCT and CCT) show potential to improve the well-being of orphans and other children made vulnerable by HIV/AIDS (OVC). We address the gap in current understanding about the extent to which household-based cash transfers differentially impact individual children’s outcomes, according to risk or protective factors such as orphan status and household assets.

**Methods:** Data were obtained from a cluster-randomised controlled trial in eastern Zimbabwe, with random assignment to three study arms - UCT, CCT or control. The sample included 5,331 children ages 6-17 from 1,697 households. Generalized linear mixed models were specified to predict OVC health vulnerability (child chronic illness and disability) and social protection (birth registration and 90% school attendance). Models included child-level risk factors (age, orphan status); household risk factors (adults with chronic illnesses and disabilities, greater
household size); and **household protective factors** (including asset-holding). Interactions were systematically tested.

Results: **Orphan status** was associated with decreased likelihood for birth registration, and paternal orphans and children for whom both parents’ survival status was unknown were less likely to attend school. In the UCT arm, paternal orphans fared better in likelihood of birth registration compared with non-paternal orphans. Effects of study arms on outcomes were not moderated by any other risk or protective factors. **High household asset-holding** was associated with decreased likelihood of child's chronic illness and increased birth registration and school attendance, but household assets did not moderate the effects of cash transfers on risk or protective factors.

**Conclusion:** **Orphaned children are at higher risk for poor social protection outcomes even when cared for in family-based settings.** UCT and CCT each produced direct effects on children’s social protection which are not moderated by other child- and household-level risk factors, but orphans are less likely to attend school or obtain birth registration. **The effects of UCT and CCT are not moderated by asset-holding, but greater household assets predict greater social protection outcomes.** Intervention efforts need to focus on ameliorating the additional risk burden carried by orphaned children. These efforts might include caregiver education, and additional incentives based on efforts made specifically for orphaned children.

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

**Editor’s notes:** In sub-Saharan Africa, there is growing evidence on the impact of cash transfers on youth HIV risk, health outcomes of orphans and other children made vulnerable by HIV and on social protection outcomes such as school attendance. Using data from a cluster randomised controlled trial in Zimbabwe, the authors sought to understand the extent to which individual level children's risk factors and household asset accumulation influence the effects of cash transfers on child health (chronic illness and disability) and child social protection (birth registration status and school attendance) outcomes.

There was no evidence to illustrate that the type of orphan status, maternal or paternal or both, was associated with child disability or chronic illness. There was some evidence that suggested that orphan status predicted social vulnerability, i.e., risk for not obtaining birth registration. However the receipt of an unconditional cash transfer buffered this risk for paternal orphans, suggesting birth registration being a gendered activity and that mothers of paternal orphans might use cash incentives to invest in the human capital of their children. Results also demonstrate that cash transfers, both unconditional and conditional, and household accumulation of assets have positive effects on social protection outcomes including birth registration and school attendance, separately. But the effect of cash transfers is not influenced by the amount of assets held by a household. Furthermore, in contrast to other studies, there is no evidence from these findings to illustrate that cash transfers have an effect on health outcomes. However, asset holding seems to have a weak, but positive effect on children’s chronic illness, but no effect on chronic disability. This suggests that households with some assets are able to use these assets to access health care services to treat chronic illness. Furthermore these households with greater assets may also experience better living conditions which perhaps contribute to better health outcomes.

Given the financial burden of HIV on households caring for orphan and vulnerable children, programme efforts for HIV prevention should focus on addressing this burden. This study contributes to the evidence base from other countries in sub-Saharan Africa. Findings from Malawi and Kenya, for example, have illustrated that the provision of cash transfers to HIV affected households provide a
substantial boost that is effective in improving outcomes among vulnerable children, in particular certain social protection outcomes, such as school attendance.

6. Eliminate stigma and discrimination

The relationship between HIV and prevalence of disabilities in sub-Saharan Africa: systematic review.


Objective: To systematically review evidence on the prevalence and risk of disabilities among children and adults living with HIV in sub-Saharan Africa.

Methods: Articles were identified from 1980 to June 2013 through searching seven electronic databases. Epidemiological studies conducted in sub-Saharan Africa that explored the association between HIV status and general disability or specific impairments, with or without an HIV-uninfected comparison group, were eligible for inclusion.

Results: Of 12 867 records initially identified, 61 papers were deemed eligible for inclusion. The prevalence of disability was high across age groups, impairment types and study locations. Furthermore, 73% of studies using an HIV-comparator found significantly lower levels of functioning in people living with HIV (PLHIV). By disability type, the results were as follows: (i) for studies measuring physical impairments (n = 14), median prevalence of limitations in mobility and motor function among PLHIV was 25.0% (95% CI: 21.8-28.2%). Five of eight comparator studies found significantly reduced functioning among PLHIV; for arthritis, two of three studies which used an HIV-comparison group found significantly increased prevalence among PLHIV; (ii) for sensory impairment studies (n = 17), median prevalence of visual impairment was 11.2% (95%CI: 9.5-13.1%) and hearing impairment was 24.1% (95%CI: 19.2-29.0%) in PLHIV. Significantly increased prevalence among PLHIV was found in one of four (vision) and three of three studies (hearing) with comparators; (iii) for cognitive impairment in adults (n = 30), median prevalence for dementia was 25.3% (95% CI: 22.0-28.6%) and 40.9% (95% CI: 37.7-44.1%) for general cognitive impairment. Across all types of cognitive impairment, twelve of fourteen studies found a significant detrimental effect of HIV infection; (iv) for developmental delay in children with HIV (n = 20), median prevalence of motor delay was 67.7% (95% CI: 62.2-73.2%). All nine studies that included a comparator found a significant difference between PLHIV and controls; for cognitive development and global delay, a significant detrimental effect of HIV was found in five of six and one of two studies, respectively. In the nine cohort studies comparing vertically infected and uninfected children, eight showed a significant gap in development over time in children with HIV. Finally, fifteen of thirty-one (48%) studies found a statistically significant dose-response relationship between indicators of disease progression (CD4 or WHO stage) and disability.

Conclusions: HIV is widespread in sub-Saharan Africa and the evidence suggests that it is linked to disabilities, affecting a range of body structures and functions. More research is needed to better understand the implications of HIV-related disability for individuals, their families as well as those working in the fields of disability and HIV so that appropriate interventions can be developed.

Abstract  Full-text [free] access
Editor's notes: As ART is scaled-up, and people living with HIV live longer, an increasing number of people will face challenges of HIV-associated disability. Disability may be partly a direct effect of living with HIV, but may also be an indirect effect, for example due to side effects of treatment. There has been relatively little research on this topic, particularly in low and middle-income countries and this is the first systematic review of the prevalence of disability among people living with HIV in sub-Saharan Africa. The review found a high prevalence of all categories of disability. The majority of studies had an HIV-negative comparison group among whom levels of disability were lower than among people living with HIV. Developmental delay was the impairment most strongly linked to HIV, with prevalence as high as 78% in children living with HIV. To minimize the chance that the observed association was due to reverse causality, the review excluded studies which clearly focused on disability as a risk factor for HIV, although it is likely that some studies still included individuals in whom disability preceded HIV infection. There was also relatively little data on ART status and duration in many studies, which may impact on the association of HIV and disability. Despite these limitations, this study highlights the need to focus on prevention and management of HIV-associated disability in sub-Saharan Africa and development of effective, low-cost evidence-informed activities.

7. Strengthening HIV integration

Sorting through the lost and found: are patient perceptions of engagement in care consistent with standard continuum of care measures?


Background: Indicators for determining one's status on the HIV care continuum are often measured using clinical and surveillance data but do not typically assess patient perspectives. We assessed patient-reported care status along the care continuum and whether it differed from medical records and surveillance data.

Methods: Between June 2013 and October 2014, a convenience sample of clinic-attending HIV-infected persons was surveyed regarding care-seeking behaviors and self-perceived status along the care continuum. Participant responses were matched to DC Department of Health surveillance data and clinic records. Participants’ care patterns were classified using Health Resources Services Administration-defined care status: in care (IC), sporadic care (SC), or out of care (OOC). Semistructured qualitative interviews were analyzed using an open coding process to elucidate relevant themes regarding participants' perceptions of engagement in care.

Results: Of 169 participants, most were male participants (64%) and black (72%), with a mean age of 50.7 years. Using self-reported visit patterns, 115 participants (68%) were consistent with being IC, 33 (20%) SC, and 21 (12%) OOC. Among OOC participants, 52% perceived themselves to be fully engaged in HIV care. In the previous year, among OOC participants, 71% reported having a non-HIV-related medical visit and 90% reported current antiretroviral use. Qualitatively, most SC and OOC persons did not see their HIV providers regularly because they felt healthy.

Conclusions: Participants' perceptions of HIV care engagement differed from actual care receipt as measured by surveillance and clinical records. Measures of care engagement may need to be reconsidered as persons not receiving regular HIV care maybe accessing other health care and HIV medications elsewhere.
Abstract access

Editor’s notes: This interesting mixed methods study examined engagement and retention in HIV care among people living with HIV in Washington DC. In addition to the convenience sample of clinic attendees listed in the abstract of the paper, data were also accessed on people who had not received clinical care in the previous 12 months, according to clinic records. These people were being focused on by a Department of Health initiative to re-engage them in care. As the clinic staff contacted people to re-engage with them they were offered the opportunity to be recruited into this study. A very helpful diagram on page S46 of this paper sets out this recruitment strategy. This sampling approach allowed the authors to compare data collected from an interviewer-administered structured survey (collecting self-reported data) with data abstracted from clinic records (with the participant’s consent) and data from Department of Health surveillance records. In addition 62 of the participants took part in in-depth interviews. In keeping with other studies on linkage to care, the authors found that participants who were considered ‘out of care’ by the Department of Health and clinic records did not necessarily consider themselves to be out of care. These were often people who were doing well and saw no need to visit the clinic regularly, particularly if, for individuals on antiretroviral therapy, they were able to access drug supplies from other sources.

The study also suggests the importance of understanding the limitations of different data sources. While the limitations of self-reported data are well known, the authors also highlight the drawback of using clinic records. The Department of Health re-engagement initiative had found that 57% of the people thought to be out of care were actually receiving care elsewhere. The authors therefore stress the importance of using a combination of data sources in care surveillance.

Many people considered to be ‘out of care’ by their clinic were surprised to have had this label applied to them. The authors suggest that this finding emphasises the need for better communication between provider and patient so that treatment goals and the importance of regular clinic visits are understood. However, they go on to say that this finding also supports the on-going process of rethinking definitions of ‘engagement in care’ to be more responsive to individual needs and perceptions. Indeed the change in the United States Department of Health and Human Services guidelines to recommend that patients who are virally suppressed can be monitored less-frequently is in keeping with this suggestion.

"...I should maintain a healthy life now and not just live as I please...": men’s health and fatherhood in rural South Africa.


This study examines the social context of men’s health and health behaviors in rural KwaZulu-Natal, South Africa, particularly in relationship to fathering and fatherhood. Individual interviews and focus groups were conducted with 51 Zulu-speaking men. Three themes related to men’s health emerged from the analysis of transcripts: (a) the interweaving of health status and health behaviors in descriptions of “good” and “bad” fathers, (b) the dominance of positive accounts of health and health status in men’s own accounts, and (c) fathers’ narratives of transformations and positive reinforcement in health behaviors. The study reveals the pervasiveness of an ideal of healthy fathers, one in which the health of men has practical and symbolic importance not only for men themselves but also for others in the family and community. The study also suggests that men hold in esteem fathers who manage to be involved with their biological children who are not coresident or who are playing a fathering role for nonbiological children.
(social fathers). In South Africa, men’s health interventions have predominantly focused on issues related to HIV and sexual health. The new insights obtained from the perspective of men indicate that there is likely to be a positive response to health interventions that incorporate acknowledgment of, and support for, men’s aspirations and lived experiences of social and biological fatherhood. Furthermore, the findings indicate the value of data on men’s involvement in families for men’s health research in sub-Saharan Africa.

Abstract access

Editor’s notes: As the authors of this paper note, a lot of research has looked at men’s sexual and health-associated behaviour as risk factors for HIV infection of their partners and themselves. Far less attention has been paid to men’s family situation and how this, and how they view their family role, shapes their health behaviours. This paper begins to fill that gap. Using data from in-depth interviews and group discussions with 51 men in KwaZulu-Natal, South Africa, the authors describe how men view themselves as ‘fathers’ and how this affects what they do. Each of the men set out what this role means for how they behave and believe other fathers should behave. While the authors note that the sample would have been biased towards men happy to talk about being a father, the results are quite striking. The men frequently described the positive things they did for their children and wanted to do for their families. They claimed their own health behaviours to be exemplary. The men compared ‘good’ fathers with ‘bad’ fathers, men who drank and were sexually promiscuous. All the respondents were ‘good’ fathers. Not one of the men disclosed their HIV-status during the interviews. The authors note that the men were much freer discussing diet, weight, smoking and alcohol than HIV. Given HIV-associated stigma and the negative stereotypes of promiscuous men spreading infection, it is hardly surprising that men constructed a positive identity through their narratives and distanced themselves from personal HIV-associated discussion. Tailored health messages which reinforce the behaviour of ‘good fathers’ are likely to have a greater impact on these men’s sexual behaviour than messages that aim to scare.