Welcome to the 3rd issue of HIV this month! In this issue, we cover the following topics:

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   - Young adults presenting with fever: consider HIV seroconversion
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7. **Strengthening HIV integration**

- Promising results from integrating depression treatment with HIV care in Cameroon
- Integrated routine screening for syphilis and HIV in antenatal care is cost-effective in China

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Peter Godfrey-Faussett and Celeste Sandoval
UNAIDS
1. Reduce sexual transmission

High percentage of recent HIV infection leading to onward transmission in Odessa, Ukraine associated with young adults.


The proportion of new HIV diagnoses between May and December 2009 across Odessa recently-infected was estimated using the BED-CEIA assay. Logistic regression models were used to explore factors associated with testing as recent. Of 1313 newly-diagnosed individuals, 321 (24 %) were classified as recent. Recent infection was less likely among older adults [odds ratio (OR) = 0.70 per 10-year increase, 95 % CI 0.60-0.82]. Compared to men residing in Odessa city, women in rural Odessa and non-resident men were more likely to be recently-infected (OR 1.85, 1.26-2.71 and 2.83, 1.15-6.97, respectively). Reason for test was not associated with recent infection. In sensitivity analysis, after excluding individuals tested due to clinical indications, the proportion recently-infected and the association with age remained virtually unchanged. Our findings suggest a high risk of onward transmission, particularly in younger age groups. These findings highlight the need for tailored prevention strategies and ongoing RITA testing to monitor and evaluate effectiveness of prevention programmes.

Abstract access

Editor’s notes: Ukraine has the highest reported rates of HIV infection in Europe. This study (part of the CASCADE collaboration) sought to estimate the proportion of new HIV diagnoses due to recent infection, using a recent infection testing algorithm (RITA). Of a total of 1313 new diagnoses, about a quarter were classified as recent infections, suggesting a high risk of onward transmission given the high levels of viraemia associated with acute HIV infection. The study highlights the move from injecting drug use as the main mode of transmission, to heterosexual intercourse. It also stresses the urgent need for focused HIV prevention strategies in the population, especially among young people (age 16-24 years).

Safety of medical male circumcision in human immunodeficiency virus-infected men in Rakai, Uganda.


Objective: To assess the safety of medical male circumcision (MMC) among human immunodeficiency virus (HIV)-infected men with CD4 levels <350 cells/mm³, CD4 counts ≥350 cells/mm³, and HIV-negative men.

Methods: Two hundred forty-two HIV-infected men and a sample of 262 HIV-negative consenting men aged 12 years or older who requested free MMC were enrolled in a prospective study. Blood for HIV testing and a CD4 count were collected before surgery. During weekly follow-up over 6 weeks, data were collected on wound healing and adverse events (AEs) by examination, and resumption of sex and condom use ascertained by interview. Surgery-related AEs were characterized by type, severity, management, and resolution. Chi-square and Fisher's exact tests were used to test for differences in AE proportions.
Results: Overall, only 2 of the 453 men experienced moderate AEs, a rate of 0.44 per 100 surgeries. No AE occurred among HIV-negative men, whereas the AE rate among HIV-infected men with CD4 counts ≥350 cells/mm³ was 0.79 per 100 surgeries, and among men with CD4 counts <350 cells/mm³ the rate was 1.19 per 100 surgeries (P = .214). AE rates were comparable for all characteristics (P > .05).

Conclusion: HIV-positive men can be safely included in MMC roll out programs without necessitating presurgery CD4 counts determination.

Abstract access

Editor's notes: This paper addresses a knowledge gap about the safety of voluntary medical male circumcision (VMMC) among HIV-positive men with a CD4 count below 350 cells/mm³. WHO recommends that men who are HIV-positive, or don’t know their status, should not be denied voluntary medical male circumcision (VMMC). However, to date there has been little data on the safety of VMMC among HIV-positive men with low CD4 counts. The study is relatively small (90 men with CD4 counts below 350 cells/mm³) amongst whom there was one, moderate adverse event (AE). One moderate AE was also seen among the 152 HIV positive men with CD4 counts above 350 cells/mm³. So whilst this data is reassuring, further data on rates of AE among HIV positive men are needed.

Acute HIV-1 infection is as common as malaria in young febrile adults seeking care in coastal Kenya.


Background: Febrile adults are usually not tested for acute HIV-1 infection (AHI) in Africa. We assessed a strategy to diagnose AHI among young adult patients seeking care.

Methods: Young adults (<30 years) who met predefined AHI criteria at care seeking, including fever, sexually transmitted disease symptoms, diarrhoea, body pains or multiple partners were referred from five pharmacies and screened at five health facilities. Prevalent HIV-1 was diagnosed by nationally recommended serial rapid HIV-1 testing. Willing HIV-1-negative patients were evaluated for AHI, defined as a positive p24 antigen test, and subsequent seroconversion or RNA detection. Febrile patients evaluated for AHI were also screened for malaria using a rapid test, with PCR confirmation of positives.

Results: In 3 602 adults seeking care, overall HIV-1 prevalence was 3.9%: 7.6% (68/897) among patients meeting AHI criteria vs. 2.6% (71/2705) among those who did not (P < 0.001). AHI was diagnosed in 5 of 506 HIV-1-negative or discordant patients who met AHI risk criteria and were completely evaluated [prevalence 1.0%, 95% confidence interval (CI) 0.3-2.3%]. Of these 5 AHI cases, 4 were diagnosed among the 241 patients with fever (prevalence 1.7%, 95% CI 0.5-4.2%), vs. 1 among 265 non-febrile patients (prevalence 0.4%, 95% CI 0.0-2.0%, P = 0.1). Malaria was confirmed by PCR in 4 (1.7%) of the 241 febrile patients.

Conclusion: AHI was as common as confirmed malaria in young febrile adults seeking care. An AHI detection strategy targeting young febrile adults seeking care at pharmacies and health facilities is feasible and should be considered as an HIV-prevention strategy in high-transmission settings.

Abstract access
Editor’s notes: People with acute HIV infection typically have high viral loads, resulting in particularly high risk of transmission. However, few people with HIV are identified during this acute illness, thus missing opportunities for activities to reduce the risk of onward transmission. The authors note that in the setting of this study, coastal Kenya, HIV incidence is relatively high and thus the frequency of acute HIV infection observed here may not be generalisable to other settings. However, the results serve as a reminder that acute HIV infection is an important differential diagnosis among adults presenting to health services with fever. Among people meeting the study criteria for possible acute HIV infection, on rapid testing 7.6% were HIV positive, illustrating the importance of provider-initiated testing and counselling. People with very recent HIV infection may be in the “window period” and thus have a negative or indeterminate HIV test result. A diagnosis of acute HIV infection could be made with a test for p24 antigen or HIV viral load, if available. In the absence of access to such tests, if acute HIV infection is suspected, HIV antibody testing should be repeated after two to four weeks. Suspected acute HIV infection provides an opportunity for counselling with a view to reducing the risk of HIV transmission and for linkage to HIV care and treatment services.

The dual impact of antiretroviral therapy and sexual behaviour changes on HIV epidemiologic trends in Uganda: a modelling study.


Objectives: Antiretroviral therapy (ART) availability in a population may influence risky sexual behaviour. We examine the potential impact of ART on the HIV epidemic, incorporating evidence for the impact that ART may have on risky sexual behaviour.

Methods: A mathematical model, parameterised using site-specific data from Uganda and worldwide literature review, was used to examine the likely impact of ART on HIV epidemiologic trends. We varied assumptions about rates of initiating ART, and changes in sexual partner turnover rates.

Results: Modelling suggests that ART will reduce HIV incidence over 20 years, and increase prevalence. Even in the optimistic scenario of ART enrollment beginning after just five months of infection (in HIV stage 2), prevalence is estimated to rise from a baseline of 10.5% and 8.3% among women and men, respectively, to at least 12.1% and 10.2%, respectively. It will rise further if sexual disinhibition occurs or infectiousness while on ART is slightly higher (2% female to male, rather than 0.5%). The conditions required for ART to reduce prevalence over this period are likely too extreme to be achievable. For example, if ART enrolment begins in HIV stage 1 (within the first 5 months of infection), and if risky sexual behaviour does not increase, then 3 of our 11 top fitting results estimate a potential drop in HIV prevalence by 2025. If sexual risk taking rises, it will have a large additional impact on expected HIV prevalence. Prevalence will rise despite incidence falling, because ART extends life expectancy.

Conclusions: HIV prevalence will rise. Even small increases in partner turnover rates will lead to an additional substantial increase in HIV prevalence. Policy makers are urged to continue HIV prevention activities, including promoting sex education, and to be prepared for a higher than previously suggested number of HIV infected people in need of treatment.

Abstract Full-text [free] access

Editor’s notes: There have been conflicting predictions from mathematical models about whether widespread antiretroviral therapy (ART) will lead to increases or decreases in HIV prevalence. These differences are likely to be partly due to different assumptions being made in the models. They are
probably also partly due to differences in the nature and maturity of the HIV epidemic in different settings. In the Ugandan setting, this analysis finds that taking into account both reduced HIV transmission and increased survival on ART, increased ART coverage is likely to result in increased HIV prevalence. (This is in qualitative agreement with historical trends, although this is not assessed here.) The authors also explore what happens if widespread ART availability leads to increased sexual activity in the general population, as suggested by previous studies in this setting. Unsurprisingly, increased sexual activity further increases HIV prevalence.

**NIMH Project Accept (HPTN 043): results from in-depth interviews with a longitudinal cohort of community members.**


**Introduction:** NIMH Project Accept (HPTN 043) is a community-randomized trial to test the safety and efficacy of a community-level intervention designed to increase testing and lower HIV incidence in Tanzania, Zimbabwe, South Africa and Thailand. The evaluation design included a longitudinal study with community members to assess attitudinal and behavioral changes in study outcomes including HIV testing norms, HIV-related discussions, and HIV-related stigma.

**Methods:** A cohort of 657 individuals across all sites was selected to participate in a qualitative study that involved 4 interviews during the study period. Baseline and 30-month data were summarized according to each outcome, and a qualitative assessment of changes was made at the community level over time.

**Results:** Members from intervention communities described fewer barriers and greater motivation for testing than those from comparison communities. HIV-related discussions in intervention communities were more grounded in personal testing experiences. A change in HIV-related stigma over time was most pronounced in Tanzania and Zimbabwe. Participants in the intervention communities from these two sites attributed community-level changes in attitudes to project specific activities.

**Discussion:** The Project Accept intervention was associated with more favorable social norms regarding HIV testing, more personal content in HIV discussions in all study sites, and qualitative changes in HIV-related stigma in two of five sites.

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

**Editor’s notes:** This paper describes a qualitative evaluation of the impact of NIMH Project Accept. The programme sought to determine the safety and efficacy of a community level behavioural intervention in reducing HIV incidence. The programme included: 1) increasing community knowledge about HIV; 2) increasing access to voluntary testing and counselling; and 3) providing post-test support services. Programme communities had higher rates of testing and improved social norms regarding HIV, than comparison communities. There was no impact on HIV-related stigma. The qualitative research collected in this evaluation describes how the quantitative changes found in the main trial happened. This paper highlights the importance of using a mixed methods approach when studying multi-level activities at the community level. The study determined that programme community participants had fewer barriers and stronger motivation for testing than comparison communities. The qualitative analysis provided a narrative for how the programmes affected the communities. There were more favourable community norms regarding HIV testing in the programme.
communities. The primary goal of Project Accept was that HIV-related stigma would be reduced but there was little quantitative evidence to support this hypothesis in the study. Qualitative evidence did show some reduction in stigmatizing language over time across all study sites. No meaningful patterns of change in sexual risk behaviour were found across the programme and comparison communities.

Where does treatment optimism fit in? Examining factors associated with consistent condom use among people receiving antiretroviral treatment in Rio de Janeiro, Brazil.

Hanif H, Bastos FI, Malta M, Bertoni N, Winch PJ, Kerrigan D. AIDS Behav. 2014 Feb 17

In the era of highly active antiretrovirals, people living with HIV (PLWH) have resumed sexual activity in the context of longer and healthier lives, and thus the chances of transmitting the HIV virus, as well as the potential to be re-infected also increase. **HIV treatment optimism has been found to be associated with sexual risk behaviors among PLWH in different settings.** A cross sectional survey was conducted to examine the relationship between treatment optimism, safer sex burnout and consistent condom use as well as variables associated with treatment optimism in a sample of PLWH on antiretrovirals (ARVs) in Rio de Janeiro, Brazil (n = 604). Seventy-two percent of participants always used a condom in the last 6 months. Homosexual, bisexual, transexual persons were less likely to use condoms consistently than heterosexuals (AOR .58 CI .42–.78). **Those who were treatment optimistic (AOR .46 CI .25–.88) were more likely not use a condom consistently in the past 6 months, as were participants who reported safer sex burnout (AOR .58 CI .36–.90).** Sexual orientation, safer sex burnout, and lower education levels were significantly associated with higher treatment optimism in multivariate analysis. Study findings highlight the need to address psychosocial factors such as treatment optimism and safer sex burnout associated with lower consistent condom use among PLWH in Rio de Janeiro, Brazil.

Abstract

**Editor’s notes:** As HIV treatment becomes increasingly accessible, people living with HIV are able to live longer, healthier lives. Since HIV treatment is life-long, over time, people could experience a sense of complacency about the need for safer sex, defined as treatment optimism in this paper, or safer sex burnout (i.e. fatigue with having to always use condoms). This study employed a cross-sectional survey to explore the relationships between treatment optimism, safer sex burnout and condom use, in addition to other variables, in six clinic populations in Brazil. The overall study population was quite diverse in age, from 19 to 67 years. The majority of the population consisted of men (68%), and reported lower levels of education and low socio-economic status on average. Interestingly, higher education, lack of religious affiliation, higher income, and longer duration of treatment were associated with treatment optimism. These kinds of associations are not unlike what we see in populations of higher socio-economic status and vaccination rates. While 75% of the population reported consistent condom use, it is possible this was over-reported. It will be important to consider treatment optimism and safer sex burnout when expanding the use of antiretroviral drugs. Strategic messaging and repeated education on the importance of consistent safer sex practices will help ensure the success of new ARV-based interventions.

2. 15 million accessing treatment

Retention in care under universal antiretroviral therapy for HIV-infected pregnant and breastfeeding women (‘Option B+’) in Malawi.
Objective: To explore the levels and determinants of loss to follow-up (LTF) under universal lifelong antiretroviral therapy (ART) for pregnant and breastfeeding women ('Option B+') in Malawi.

Design, setting, and participants: We examined retention in care, from the date of ART initiation up to 6 months, for women in the Option B+ program. We analysed nationwide facility-level data on women who started ART at 540 facilities (n = 21,939), as well as individual-level data on patients who started ART at 19 large facilities (n = 11,534).

Results: Of the women who started ART under Option B+ (n = 21,939), 17% appeared to be lost to follow-up 6 months after ART initiation. Most losses occurred in the first 3 months of therapy. Option B+ patients who started therapy during pregnancy were five times more likely than women who started ART in WHO stage 3/4 or with a CD4 cell count 350 cells/µl or less, to never return after their initial clinic visit [odds ratio (OR) 5.0, 95% confidence interval (CI) 4.2-6.1]. Option B+ patients who started therapy while breastfeeding were twice as likely to miss their first follow-up visit (OR 2.2, 95% CI 1.8-2.8). LTF was highest in pregnant Option B+ patients who began ART at large clinics on the day they were diagnosed with HIV. LTF varied considerably between facilities, ranging from 0 to 58%.

Conclusion: Decreasing LTF will improve the effectiveness of the Option B+ approach. Tailored interventions, like community or family-based models of care could improve its effectiveness.

Abstract access

Editor’s notes: “Option B+” refers to the strategy of starting combination antiretroviral therapy (ART) for pregnant women who are HIV positive, and then continuing ART lifelong. This strategy has many advantages from a programmatic perspective, including maintaining the mother’s health and reducing the risk of transmission in future pregnancies and to HIV-negative partners. Implementation of option B+ has increased ART coverage among pregnant women in Malawi, an important positive outcome. However, the full benefits of this strategy will only be realised if women remain in care and sustain virologic suppression. These data on retention are therefore important for programme managers.

Some 17% of women who started antiretroviral therapy during pregnancy were lost to follow-up by six months. Women starting ART during pregnancy were almost five times more likely never to return after the first visit, compared to women starting ART for their own health (based on a CD4 count below 350 or WHO stage three or four). These women are of particular concern because their loss from programme likely reflects a missed opportunity to prevent HIV transmission to their children. Effective strategies to maximise retention in care need to be identified and implemented.

On a methodological note, in this analysis, loss to follow-up was defined as missing a visit by more than 60 days, whereas WHO recommends a cut-off of 90 days. This illustrates the need for ART programmes to report standardised outcomes in order to facilitate comparisons.

Impact of geographic and transportation-related barriers on HIV outcomes in sub-Saharan Africa: a systematic review.

Lankowski AJ, Siedner MJ, Bangsberg DR, Tsai AC. AIDS Behav. 2014 Feb 23. [Epub ahead of print]
Difficulty obtaining reliable transportation to clinic is frequently cited as a barrier to HIV care in sub-Saharan Africa (SSA). Numerous studies have sought to characterize the impact of geographic and transportation-related barriers on HIV outcomes in SSA, but to date there has been no systematic attempt to summarize these findings. In this systematic review, we summarized this body of literature. We searched for studies conducted in SSA examining the following outcomes in the HIV care continuum: (1) voluntary counseling and testing, (2) pre-antiretroviral therapy (ART) linkage to care, (3) loss to follow-up and mortality, and (4) ART adherence and/or viral suppression. We identified 34 studies containing 52 unique estimates of association between a geographic or transportation-related barrier and an HIV outcome. There was an inverse effect in 23 estimates (44 %), a null association in 26 (50 %), and a paradoxical beneficial impact in 3 (6 %). We conclude that geographic and transportation-related barriers are associated with poor outcomes across the continuum of HIV care.

Abstract

Editor’s notes: This systematic review focuses on the importance of structural barriers to uptake of HIV treatment and care. Specifically, these are the association between geographic and transportation-related barriers and poor outcomes among HIV positive persons. Most of the quantitative and qualitative evidence reviewed in this paper (from 66 studies in sub-Saharan Africa) support the authors’ hypothesis that geographic and transportation-related barriers contribute to poor outcomes in HIV-positive individuals at all points along the continuum of HIV care. These were indexed in terms of voluntary counselling and testing, pre-antiretroviral therapy linkage to care, loss to follow-up, and adherence and/or viral suppression. A lack of association between these barriers and HIV services use was more common in studies where the study had clear limitations. For example, the use of self-reported as opposed to objective measures of exposures, small sample sizes, and the lack of control for confounding variables. The study has important policy implications related to the decentralisation of HIV treatment and care services, point-of-care services delivery, the provision of transportation stipends, the simplification of management protocols, and the reduction in the frequency of follow up visits.

A novel community health worker tool outperforms WHO clinical staging for assessment of antiretroviral therapy eligibility in a resource-limited setting.


The accuracy of a novel community health worker antiretroviral therapy eligibility assessment tool was examined in community members in Blantyre, Malawi. Nurses independently performed World Health Organization (WHO) staging and CD4 counts. One hundred ten (55.6%) of 198 HIV-positive participants had a CD4 count of <350 cells per cubic millimeter. The community health worker tool significantly outperformed WHO clinical staging in identifying CD4 count of <350 cells per cubic millimeter in terms of sensitivity (41% vs. 19%), positive predictive value (75% vs. 68%), negative predictive values (53% vs. 47%), and area under the receiver-operator curve (0.62 vs. 0.54; P = 0.017). Reliance on WHO staging is likely to result in missed and delayed antiretroviral therapy initiation.

Abstract access

Editor’s notes: Antiretroviral Therapy (ART) eligibility assessment has been identified as one of the bottlenecks in the HIV care cascade that limits and/or delays progression of patients to starting ART.
Laboratory-based CD4 count testing requires more than one visit and is unavailable in many settings. WHO staging is difficult and time-consuming for many health care workers to use. Simplified eligibility tools are needed to simplify both facility-based and community-based ART initiation. This study found that a clinical tool incorporating a series of simple questions had greater accuracy than WHO staging, for identifying those eligible for ART, when used by community health care workers in Malawi.

Efficacy of 400 mg efavirenz versus standard 600 mg dose in HIV-infected, antiretroviral-naive adults (ENCORE1): a randomised, double-blind, placebo-controlled, non-inferiority trial.


Background: The optimum dose of key antiretroviral drugs is often overlooked during product development. The ENCORE1 study compared the efficacy and safety of reduced dose efavirenz with standard dose efavirenz in combination with tenofovir and emtricitabine as first-line treatment for HIV infection. An effective and safe reduced dose could yield meaningful cost savings.

Methods: ENCORE1 is a continuing non-inferiority trial in HIV-1-infected antiretroviral-naive adults in 38 clinical sites in 13 countries. Participants (plasma HIV-RNA >1000 log_{10} copies per mL, CD4 T-cell count 50-500 cells per µL) were randomly assigned by a computer-generated sequence with a blocking factor of four (stratified by clinical site and by screening viral load) to receive tenofovir plus emtricitabine with either a reduced daily dose (400 mg) or a standard dose (600 mg) of efavirenz. Participants, physicians, and all other trial staff were masked to treatment group. The primary endpoint was the difference in proportions of participants with plasma HIV-RNA of less than 200 copies per mL at 48 weeks. Treatment groups were regarded as non-inferior if the lower limit of the 95% CI for the difference in viral load was less than -10% by modified intention-to-treat analysis. Adverse events were summarised by treatment.

Findings: The modified intention-to-treat analysis consisted of 630 patients (efavirenz 400=321; efavirenz 600=309). 32% were women; 37% were African, 33% were Asian, and 30% were white. The mean baseline CD4 cell count was 273 cells per µL (SD 99) and median plasma HIV-RNA was 4.75 log_{10} copies per mL (IQR 0.88). The proportion of participants with a viral load below 200 copies per mL at week 48 was 94.1% for efavirenz 400 mg and 92.2% for 600 mg (difference 1.85%, 95% CI -2.1 to 5.79). CD4 T-cell counts at week 48 were significantly higher for the 400 mg group than for the 600 mg group (mean difference 25 cells per µL, 95% CI 6-44; p=0.01). We recorded no difference in grade or number of patients reporting adverse events (efavirenz 400=89.1%, efavirenz 600=88.4%; difference 0.75%, 95% CI -4.19 to 5.69; p=0.77). Study drug-related adverse events were significantly more frequent in the 600 mg group than in the 400 mg group (146% [47] vs 118 [37]), difference -10.5%, 95% CI -18.2 to -2.8; p=0.01) and significantly fewer patients with these events stopped treatment (400 mg=6 [2%], 600 mg=18 [6%], difference -3.96%, 95% CI -6.96 to -0.95; p=0.01).

Interpretation: Our findings suggest that a reduced dose of 400 mg efavirenz is non-inferior to the standard dose of 600 mg, when combined with tenofovir and emtricitabine during 48 weeks in ART-naive adults with HIV-1 infection. Adverse events related to the study drug were more frequent with 600 mg efavirenz than with 400 mg. Lower dose efavirenz should be recommended as part of routine care.

Abstract access

Editor’s notes: Nearly 10 million people in low- and middle-income countries were receiving antiretroviral therapy (ART) by the end of 2012, with plans to expand coverage to 15 million by 2015.
Several challenges must be overcome if this target is to be achieved. One of the most pertinent of these is how to fund this expansion in the current economic climate. Significant progress has already been made in reducing the cost of first-line drugs. The authors of this paper propose an alternative approach to lowering drug costs, namely dose reduction.

Evidence supporting the 600mg dose of efavirenz used in clinical practice is weak, with no difference found in the proportion of patients achieving viral suppression in the original dose finding trials of 200mg, 400mg and 600mg (unpublished). This trial in ART-naive individuals found that 400mg was non-inferior to 600mg of efavirenz in terms of viral suppression over 48 weeks of follow-up. Findings were similar when stratified by ethnic group (African, Asian, other) and body mass index, both factors which influence drug concentrations. Furthermore, fewer patients on 400mg reported adverse events which were related to efavirenz, and fewer patients with drug-related side effects on this dose stopped efavirenz. These promising results support a dose reduction strategy. However, longer term outcomes need to be evaluated and efficacy studies in patients with tuberculosis are needed before the 400mg dose is recommended for use in routine clinical practice. Certainly, if drug companies agree to manufacture this dose at scale, preferably in fixed-dose combination tablets, cost-savings could be considerable.

Text message intervention designs to promote adherence to antiretroviral therapy (ART): a meta-analysis of randomized controlled trials.


Background: The efficacy of antiretroviral therapy depends on patient adherence to a daily medication regimen, yet many patients fail to adhere at high enough rates to maintain health and reduce the risk of transmitting HIV. Given the explosive global growth of cellular-mobile phone use, text-messaging interventions to promote adherence are especially appropriate. This meta-analysis synthesized available text messaging interventions to promote antiretroviral therapy adherence in people living with HIV.

Methods: We performed Boolean searches of electronic databases, hand searches of recent year conference abstracts and reverse searches. Included studies (1) targeted antiretroviral therapy adherence in a sample of people living with HIV, (2) used a randomized-controlled trial design to examine a text messaging intervention, and (3) reported at least one adherence measurement or clinical outcome.

Results: Eight studies, including 9 interventions, met inclusion criteria. Text-messaging interventions yielded significantly higher adherence than control conditions (OR = 1.39; 95% CI = 1.18, 1.64). Sensitivity analyses of intervention characteristics suggested that studies had larger effects when interventions (1) were sent less frequently than daily, (2) supported bidirectional communication, (3) included personalized message content, and (4) were matched to participants’ antiretroviral therapy dosing schedule. Interventions were also associated with improved viral load and/or CD4+ count (k = 3; OR = 1.56; 95% CI = 1.11, 2.20).

Conclusions: Text-messaging can support antiretroviral therapy adherence. Researchers should consider the adoption of less frequent messaging interventions with content and timing that is individually tailored and designed to evoke a reply from the recipient. Future research is needed in order to determine how best to optimize efficacy.

Abstract Full-text [free] access
Editor’s notes: Adherence to antiretroviral therapy (ART) is crucial for good clinical outcomes and for reducing the risk of onward HIV transmission. In the last decade, there has been a massive increase in cellular phone ownership. This provides a promising and potentially cost-effective approach to improving ART adherence through short messaging services (SMS). The World Health Organization guidelines recommend using SMS as part of a package of activities to support adherence to ART.

This meta-analysis examined how SMS can be optimally used to promote successful adherence. Eight randomised controlled trials from the USA, Brazil, Kenya and Cameroon investigated nine types of SMS activities. Studies used multiple methods to measure adherence including self-report, electronic drug monitoring and pill counts. Overall, text messaging significantly improved the average adherence outcome. Only three of the eight studies used virologic suppression as an outcome measure; importantly these studies did show an improvement in adherence. The study highlighted the components of SMS activities that were associated with the most effect on adherence. These included less frequent messaging than daily, personalised message content, SMS matched to dosing schedules and bidirectional communication between the care provider and the participant.

In summary, SMS is a promising activity for supporting adherence, although the effect on adherence is modest. Several questions remain to be answered, namely the optimum way of operationalising this as an adherence support activity, its sustainability and its cost-effectiveness (given the modest effect size). Finally, a major limitation of ART adherence studies is the common use of non-biological measures of adherence, which do not always reflect virologic suppression. Virologic suppression is the most persuasive outcome for evaluations of programmes to improve adherence.

3. Avoid TB deaths

The effect of HIV and antiretroviral therapy on characteristics of pulmonary tuberculosis in northern Malawi: a cross-sectional study.


Background: HIV infection reduces the likelihood that individuals with pulmonary tuberculosis are smear positive and that they have cavitatory disease. Antiretroviral therapy (ART) may shift the pattern of disease to be more similar to that of HIV negative patients. This would aid diagnosis - which often depends on sputum smears - but would also increase infectiousness. We assessed the effect of HIV and ART on smear positivity and cavitatory disease in laboratory-confirmed pulmonary TB patients.

Methods: Three sputum samples were collected per pulmonary TB suspect and were examined using microscopy and culture. Chest radiographs were available for a subset of patients as part of another study. The effect of HIV and ART status on sputum smear positivity and lung cavitation were evaluated using multivariable logistic regression.

Results: Of 1 024 laboratory-confirmed pulmonary TB patients who were identified between January 2005 and December 2011, 766 had HIV and ART status available. Positive sputum smears were significantly more common among HIV negative individuals than HIV positive individuals (adjusted OR = 2.91, 95% CI 1.53 - 5.55). Compared to those HIV positive but not on ART, patients on ART were more likely to be smear positive (adjusted OR = 2.33, 95% CI 1.01 - 5.39) if they had been on ART ≤ 6 months, but only slightly more likely to be smear positive (adjusted OR = 1.43, 95% CI 0.68 - 2.99) if they were on ART > 6 months. HIV negative patients were more likely than HIV positive patients to have cavitatory disease (adjusted OR = 1.97, 95% CI
Patients on ART > 6 months had a slight increase in cavitatory disease compared to HIV positive patients not on ART (adjusted OR = 1.68, CI 0.78 - 3.63).

Conclusion: HIV infection is associated with less smear positivity and cavitation in pulmonary TB patients. Among HIV positive patients, the use of ART shifts the presentation of disease towards that seen in HIV-negative individuals, which facilitates diagnosis but which also could increase infectiousness.

Abstract Full-text [free] access

Editor’s notes: Attenuation of immune responses to Mycobacterium tuberculosis reduces pulmonary immunopathology in patients with HIV co-infection. This decreases the risk of pulmonary cavitiation and of testing sputum smear positive on microscopy. Having confirmed these associations, this study further demonstrated that antiretroviral therapy (ART) reverses this association. ART was associated with increased risk of pulmonary cavitiation and sputum smear-positivity, likely reflecting restoration of immunopathology. TB cases developing during ART may therefore be more infectious, which has important implications for TB transmission risk.

4. Close the resource gap

Confronting 'scale-down': Assessing Namibia’s human resource strategies in the context of decreased HIV/AIDS funding.


In Namibia, support through the Global Fund and President’s Emergency Plan for AIDS Relief has facilitated an increase in access to HIV and AIDS services over the past 10 years. In collaboration with the Namibian government, these institutions have enabled the rapid scale-up of prevention, treatment and care services. Inadequate human resources capacity in the public sector was cited as a key challenge to initial scale-up; and a substantial portion of donor funding has gone towards the recruitment of new health workers. However, a recent scale-down of donor funding to the Namibian health sector has taken place, despite the country’s high HIV and AIDS burden. With a specific focus on human resources, this paper examines the extent to which management processes that were adopted at scale-up have proven sustainable in the context of scale-down. Drawing on data from 43 semi-structured interviews, we argue that human resources planning and management decisions made at the onset of the country’s relationship with the two institutions appear to be primarily driven by the demands of rapid scale-up and counter-productive to the sustainability of interventions.

Abstract access

Editor’s notes: Some countries graduate to higher income categories and become ineligible for funding from major donors, such as the Global Fund and PEPFAR. As this happens, it is increasingly important to draw lessons on how to manage this transition from international to domestic financing and ownership. Using the case of human resource management, this study underscores the need to establish exit strategies early on. It also emphasises the need to ensure the integration of management processes within government systems. These are deemed necessary if high service coverage rates are to be maintained. The case study documents how additional health professionals were recruited at higher salaries than government salaries through a parallel recruitment system.
This was done in order to meet the needs of service scale-up. However, that approach led to an unsustainable situation. Sudden salary cuts jeopardised service continuity and the expectation that these staff would be absorbed on to the government payroll. There appears to be a trade-off between certain structures to enable rapid scale-up and programme sustainability. These ought to be planned for at an early stage of funding partnerships.

After the Global Fund: Who can sustain the HIV/AIDS response in Peru and how?

Peru has received around $70 million from the Global Fund to fight AIDS, Tuberculosis and Malaria (Global Fund). Recent economic growth resulted in grant ineligibility, enabling greater government funding, yet doubts remain concerning programme continuity. This study examines the transition from Global Fund support to increasing national HIV/AIDS funding in Peru (2004–2012) by analysing actor roles, motivations and effects on policies, identifying recommendations to inform decision-makers on priority areas. A conceptual framework, which informed data collection, was developed. Thirty-five in-depth interviews were conducted from October to December 2011 in Lima, Peru, among key stakeholders involved in HIV/AIDS work. Findings show that Global Fund involvement led to important breakthroughs in the HIV/AIDS response, primarily concerning treatment access, focus on vulnerable populations and development of a coordination body. Nevertheless, reliance on Global Fund financing for prevention activities via non-governmental organisations, compounded by lack of government direction and weak regional governance, diluted power and caused role uncertainty. Strengthening government and regional capacity and fostering accountability mechanisms will facilitate an effective transition to government-led financing. Only then can achievements gained from the Global Fund presence be maintained, providing lessons for countries seeking to sustain programmes following donor exit.

Abstract access

Editor's notes: Some countries graduate to higher income categories and become ineligible for funding from major donors, such as the Global Fund and PEPFAR. As this happens, it is important to learn how the transition from international to domestic financing and ownership is managed. This study complements the previous paper, and documents the case of Peru and the impending exit of Global Fund support. The national and regional coordination bodies initially created for inter-sectoral dialogue and planning around Global Fund grant applications appear to be enabling factors for programme sustainability. As Peru started aligning Global Fund HIV activities with local priorities early on, this has helped set the stage for a smoother integration of such efforts in the national response. The authors highlight, however, that the predominant role of NGOs as implementers of prevention activities could become a limiting factor for sustainability. This is so, given that they will become dependent on government funding, and may have a weakened ability to be able to hold the government to account.

5. Eliminate gender inequalities

Intimate partner violence and HIV infection among women: a systematic review and meta-analysis.
Introduction: To assess evidence of an association between intimate partner violence (IPV) and HIV infection among women.

Methods: Medline/PubMed, Embase, Web of Science, EBSCO, Ovid, Cochrane HIV/AIDS Group's Specialized Register and Cochrane Central Register of Controlled Trials were searched up to 20 May 2013 to identify studies that examined the association between IPV and HIV infection in women. We included studies on women aged ≥15 years, in any form of sexually intimate relationship with a male partner.

Results: Twenty-eight studies [(19 cross-sectional, 5 cohorts and 4 case-control studies)] involving 331,468 individuals in 16 countries - the US (eight studies), South Africa (four studies), East Africa (10 studies), India (three studies), Brazil (one study) and multiple low-income countries (two studies)] were included. Results were pooled using RevMan 5.0. To moderate effect estimates, we analyzed all data using the random effects model, irrespective of heterogeneity level. Pooled results of cohort studies indicated that physical IPV [pooled RR (95% CI): 1.22 (1.01, 1.46)] and any type of IPV [pooled RR (95% CI): 1.28 (1.00, 1.64)] were significantly associated with HIV infection among women. Results of cross-sectional studies demonstrated significant associations of physical IPV with HIV infection among women [pooled OR (95% CI): 1.44 (1.10, 1.87)]. Similarly, results of cross-sectional studies indicated that combination of physical and sexual IPV [pooled OR (95% CI): 2.00 (1.24, 3.22) and any type of IPV [pooled OR (95% CI): 1.41 (1.16, 1.73)] were significantly associated with HIV infection among women.

Conclusions: Available evidence suggests a moderate statistically significant association between IPV and HIV infection among women. To further elucidate the strength of the association between IPV and HIV infection among women, there is a need for high-quality follow-up studies conducted in different geographical regions of the world, and among individuals of diverse racial/cultural backgrounds and varying levels of HIV risks.

Abstract Full-text [free] access

Editor's notes: Globally, an estimated 30% of partnered women will experience physical and/or sexual violence. As well as being a violation of human rights, there is growing evidence about the different ways in which violence and the fear of violence may limit women’s ability to prevent themselves from acquiring infection, or access services. This paper presents a systematic review and meta-analysis of current evidence on whether exposures to violence by an intimate partner increase women’s HIV risk. Commonly, debates on this issue focus on forced sex. The findings suggest that the issue is more complex – with exposures to physical violence also being associated with increased HIV risk. Exposures to both physical and sexual violence by partners, which is an indicator of more severe partner violence, found stronger effect estimates. The pathways underlying the documented associations may be multiple: as well as forced sex, women may have difficulties negotiating condom use or accessing services. Other studies have suggested that there may also be other characteristics of the relationship. These are that men who are violent are also more likely to have other risk behaviours such as problematic alcohol use or multiple sexual partners. These result in them being more likely to be HIV positive than non-violent men. The findings suggest that violence prevention activities may reduce HIV risk. They also highlight the need to ensure that HIV services are sensitive to, and able to support, women who have experienced or fear violence.
6. Eliminate stigma and discrimination

The prevalence of human immunodeficiency virus and sexually transmitted infections among female sex workers in Shiraz, South of Iran: by respondent-driven sampling.


As a concentrated epidemic, human immunodeficiency virus (HIV) is spreading rapidly in one or more groups in Iran, but in the general population its prevalence is relatively low. Female sex workers (FSWs) and their partners are at greater risk for HIV infection. To determine the prevalence of HIV and sexually transmitted infections (STIs) including gonorrhoea, chlamydia, herpes simplex type 2 and syphilis among FSWs. We conducted a cross-sectional study of 278 FSWs in Shiraz, by using respondent-driven sampling, from June to March 2010. The recruitment chain started with 14 seeds, and FSWs were tested for HIV, syphilis, herpes simplex type 2, gonorrhoea and chlamydia. HIV prevalence was 4.7% (13/278); the most prevalent STI was herpes simplex type 2, 9.7% (27/278), followed by chlamydia 9% (25/278), gonorrhoea 1.4% (4/278) and syphilis (0/278). The FSWs reported drug use (69.9%) of which 16.4% had history of injecting drug use. Unprotected sex in the past month was reported by 24.4% of FSWs. Urgent education and risk reduction programmes are needed in this population.

Abstract access

Editor’s notes: This paper describes the first cross-sectional study on HIV prevalence in female sex workers (FSWs) in Shiraz city in Iran. This city has some of the highest rates of HIV, sexually transmitted infections (STIs), and drug use in the country. The study was conducted using respondent driven sampling. Despite a fairly aggressive seeding strategy and a relatively long timeline, the study population was 278. The sample is reported to have reached equilibrium at this number; however it is unclear whether the seeds reflected the diversity of the population. FSWs are considered a hidden population in Iran, which could make it difficult to fully comprehend the depth of diversity within this group. Cultural, religious, and legal contexts in Iran make it difficult to reach populations such as FSWs, with health services and education. This can account for the growth in rates of HIV and other STIs in this population, and in Iran more generally. Overall, cases in HIV are estimated to rise in the country from 89 000 in 2009 to 106 000 in 2014. The HIV prevalence in this study was measured at 4.7%, with high rates of drug abuse at 69.9%. As expected, drug use was highly correlated with HIV prevalence. HSV-2 and gonorrhoea were the most prevalent STIs. FSWs reported fairly low rates of condom use overall, and as in other populations of FSWs, higher rates were seen with clients than with regular partners. Additionally, low rates of condom use were reported, especially for anal and oral sex. This important study sheds light on an otherwise hidden population and highlights the need for education and outreach of health services tailored to this population.

7. Strengthening HIV integration

Feasibility, safety, acceptability, and preliminary efficacy of measurement-based care depression treatment for HIV patients in Bamenda, Cameroon.


Depression affects 18-30 % of HIV-infected patients in Africa and is associated with greater stigma, lower antiretroviral adherence, and faster disease progression. However, the region’s
health system capacity to effectively identify and treat depression is limited. Task-shifting models may help address this large mental health treatment gap. **Measurement-Based Care (MBC)** is a task-shifting model in which a Depression Care Manager guides a non-psychiatric (e.g., HIV) provider in prescribing and managing antidepressant treatment. We adapted MBC for depressed HIV-infected patients in Cameroon and completed a pilot study to assess feasibility, safety, acceptability, and preliminary efficacy. We enrolled 55 participants; all started amitriptyline 25-50 mg daily at baseline. By 12 weeks, most remained at 50 mg daily (range 25-125 mg). Median (interquartile range) PHQ-9 depressive severity scores declined from 13 (12-16) (baseline) to 2 (0-3) (week 12); 87% achieved depression remission (PHQ-9 <5) by 12 weeks. Intervention fidelity was high: HIV providers followed MBC recommendations at 96% of encounters. Most divergences reflected a failure to increase dose when indicated. No serious and few bothersome side effects were reported. Most suicidality (prevalence 62% at baseline; 8% at 12 weeks) was either passive or low-risk. Participant satisfaction was high (100%), and most participants (89%) indicated willingness to pay for medications if MBC were implemented in routine care. The adapted MBC intervention demonstrated high feasibility, safety, acceptability, and preliminary efficacy in this uncontrolled pilot study. Further research should assess whether MBC could improve adherence and HIV outcomes in this setting.

**Abstract access**

**Editor’s notes:** Task sharing for mental health care services has been shown effective for the general population in several low-income settings. However, its effectiveness for an HIV-positive population remains in question. By supervising HIV physicians in the provision of depression care, there is increased access to a critical mental health service. In addition, there are likely to be positive effects for HIV treatment outcomes. The results of this study provide compelling grounds for further research, specifically for a randomized control trial of the Measurement-Based Care treatment protocol.

**Cost-effectiveness of integrated routine offering of prenatal HIV and syphilis screening in China.**


Background: In China, recent rises in syphilis and HIV cases have increased the focus on preventing mother-to-child transmission of these infections. We assess the health and economic outcomes of different strategies of prenatal HIV and syphilis screening from the local health department’s perspective.

Methods: A Markov cohort decision analysis model was used to estimate the health and economic outcomes of pregnancy using disease prevalence and cost data from local sources and, if unavailable, from published literature. Adverse pregnancy outcomes included induced abortion, stillbirth, low birth weight, neonatal death, congenital syphilis in live-born infants, and perinatal HIV infection. We examined 4 screening strategies: no screening, screening for HIV only, for syphilis only, and for both HIV and syphilis. We estimated disability-adjusted life years (DALYs) for each health outcome using life expectancies and infections for mothers and newborns.

Results: For a simulated cohort of 10 000 pregnant women (0.07% prevalence for HIV and 0.25% for syphilis; 10% of HIV-positives were coinfected with syphilis), the estimated costs per DALY prevented were as follows: syphilis-only, $168; HIV-and-syphilis, $359; and HIV-only, $5 636. The estimated incremental cost-effectiveness ratio if an existing HIV-only strategy
added syphilis screening (i.e., move from the HIV-only strategy to the HIV-and-syphilis strategy) was $140 per additional DALY prevented.

Conclusions: Given the increasing prevalence of syphilis and HIV among pregnant women in China, prenatal HIV screening programs that also include syphilis screening are likely to be substantially more cost-effective than HIV screening alone and prevent many more adverse pregnancy outcomes.

Abstract access

Editor’s notes: This study uses a Markov cohort model to estimate the cost-effectiveness of combined HIV and syphilis screening in antenatal care, as compared to HIV-only screening, syphilis-only screening, or no screening. This is the first study to examine cost-effectiveness of antenatal syphilis screening in China. This is particularly interesting as existing studies modelling the cost-effectiveness of syphilis screening in antenatal care have largely focused on settings with high syphilis prevalence amongst pregnant women, such as sub-Saharan Africa. This study found that even in a low syphilis prevalence setting, combined HIV/syphilis screening is substantially cost-effective at $359 per DALY averted, and more cost-effective than HIV-only screening.