Welcome to **HIV this month!** In this issue, we cover the following topics:

1. **Reduce sexual transmission**
   - Per-act HIV transmission risk during anal sex may be higher than previously thought
   - Identifying people most likely to benefit from HIV pre-exposure prophylaxis
   - Combination prevention: the key to effective long term HIV prevention in serodiscordant couples
   - HIV-related tweeting: social media for HIV prevention?

2. **Prevent HIV among drug users**
   - Harm reduction services in Tehran: uptake and barriers

3. **15 million accessing treatment**
   - High mortality in people taking antiretroviral therapy with delayed switching following virologic failure
   - WHO clinical staging misses a significant proportion of antiretroviral therapy eligible individuals
   - Decentralization of HIV care and treatment in Kenya

4. **Avoid TB deaths**
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6. **Eliminate gender inequalities**
   - Widow cleansing and inheritance practices amongst the Luo limit women’s options to use current HIV prevention methods
• Female sex workers exposed to community mobilization less exposed to sexually transmitted infections
• Does land ownership by women reduce HIV risk?

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

Estimating per-act HIV transmission risk: a systematic review.

Background: Effective HIV prevention programs rely on accurate estimates of the per-act risk of HIV acquisition from sexual and parenteral exposures. We updated the previous risk estimates of HIV acquisition from parenteral, vertical, and sexual exposures, and assessed the modifying effects of factors including condom use, male circumcision, and antiretroviral therapy.

Methods: We conducted literature searches to identify new studies reporting data regarding per-act HIV transmission risk and modifying factors. Of the 7339 abstracts potentially related to per-act HIV transmission risk, three meta-analyses provided pooled per-act transmission risk probabilities and two studies provided data on modifying factors. Of the 8119 abstracts related to modifying factors, 15 relevant articles, including three meta-analyses, were included. We used fixed-effects inverse-variance models on the logarithmic scale to obtain updated estimates of certain transmission risks using data from primary studies, and employed Poisson regression to calculate relative risks with exact 95% confidence intervals for certain modifying factors.

Results: Risk of HIV transmission was greatest for blood transfusion, followed by vertical exposure, sexual exposures, and other parenteral exposures. Sexual exposure risks ranged from low for oral sex to 138 infections per 10 000 exposures for receptive anal intercourse. Estimated risks of HIV acquisition from sexual exposure were attenuated by 99.2% with the dual use of condoms and antiretroviral treatment of the HIV-infected partner.

Conclusion: The risk of HIV acquisition varied widely, and the estimates for receptive anal intercourse increased compared with previous estimates. The risk associated with sexual intercourse was reduced most substantially by the combined use of condoms and antiretroviral treatment of HIV-infected partners.

Abstract access

Editor’s notes: The study updates the 2005 Centres for Disease Control (CDC) per-act HIV transmission risks with estimates from recent publications. In addition, it summarizes the effects of various co-factors that modify the transmission risks during sexual exposure. These include genital ulcer disease, viral load, disease stage, use of antiretrovirals, condom use and male circumcision. However, estimates from low-income countries on sexual and mother-to-child transmission are very heterogeneous and not included in the analyses. In general, the updated estimates of transmission risks are comparable to figures from the 2005 CDC study. But they also suggest that the transmission probabilities for both receptive and insertive anal intercourse could be higher than previously thought. Further, the study reasserts that the per-act risk for all sexual exposures is substantially attenuated through the use of condoms and antiretrovirals. These new estimates will be important for both modelling studies and prevention programmes. But a better understanding of HIV transmission risks in low-income countries is needed.

HIV pre-exposure prophylaxis in men who have sex with men and transgender women: a secondary analysis of a phase 3 randomised controlled efficacy trial.
Background: For maximum effect pre-exposure prophylaxis should be targeted to the subpopulations that account for the largest proportion of infections (population-attributable fraction [PAF]) and for whom the number needed to treat (NNT) to prevent infection is lowest. We aimed to estimate the PAF and NNT of participants in the iPrEx (Pre-Exposure Prophylaxis Initiative) trial.

Methods: The iPrEx study was a randomised controlled efficacy trial of pre-exposure prophylaxis with coformulated tenofovir disoproxil fumarate and emtricitabine in 2 499 men who have sex with men (MSM) and transgender women. Participants aged 18 years or older who were male at birth were enrolled from 11 trial sites in Brazil, Ecuador, Peru, South Africa, Thailand, and the USA. Participants were randomly assigned (1:1) to receive either a pill with active pre-exposure prophylaxis or placebo, taken daily. We calculated the association between demographic and risk behaviour during screening and subsequent seroconversion among placebo recipients using a Poisson model, and we calculated the PAF and NNT for risk behaviour subgroups.

Findings: Patients were enrolled between July 10, 2007, and Dec 17, 2009, and were followed up until Nov 21, 2010. Of the 2 499 MSM and transgender women in the iPrEx trial, 1 251 were assigned to pre-exposure prophylaxis and 1 248 to placebo. 83 of 1 248 patients in the placebo group became infected with HIV during follow-up. Participants reporting receptive anal intercourse without a condom seroconverted significantly more often than those reporting no anal sex without a condom (adjusted hazard ratio [AHR] 5.11, 95% CI 1.55-16.79). The overall PAF for MSM and transgender women reporting receptive anal intercourse without a condom was 64% (prevalence 60%). Most of this risk came from receptive anal intercourse without a condom with partners with unknown serostatus (PAF 53%, prevalence 54%, AHR 4.76, 95% CI 1.44-15.71); by contrast, the PAF for receptive anal intercourse without a condom with an HIV-positive partner was 1% (prevalence 1%, AHR 7.11, 95% CI 0.70-72.75). The overall NNT per year for the cohort was 62 (95% CI 44-147). NNTs were lowest for MSM and transgender women self-reporting receptive anal intercourse without a condom (NNT 36), cocaine use (12), or a sexually transmitted infection (41). Having one partner and insertive anal sex without a condom had the highest NNTs (100 and 77, respectively).

Interpretation: Pre-exposure prophylaxis may be most effective at a population level if targeted toward MSM and transgender women who report receptive anal intercourse without a condom, even if they perceive their partners to be HIV negative. Substance use history and testing for STIs should also inform individual decisions to start pre-exposure prophylaxis. Consideration of the PAF and NNT can aid in discussion of the benefits and risks of pre-exposure prophylaxis with MSM and transgender women.

Abstract access

Editor’s notes: Pre-exposure prophylaxis (PreP) is the only biomedical prevention activity shown to be effective against acquisition of HIV in men who have sex with men (MSM) and transgender women, in a randomised controlled trial. The US Centers for Disease Control (CDC) and WHO recommend PreP for MSM and transgender women at high risk of HIV infection. However, many health care providers have difficulty assessing risk and neither the CDC nor WHO has yet provided specific behavioural criteria for when to use pre-exposure prophylaxis. The purpose of this study was to identify subpopulations of participants within the iPrEx trial, for whom PreP may have the largest effect on HIV prevention. The findings suggest that MSM and transgender women can be screened for potential eligibility for PreP in clinical practice by asking about recent receptive anal intercourse
without a condom. Substance use history and testing for sexually transmitted infections should also be considered, to inform individual decisions to start pre-exposure prophylaxis.

HIV sexual transmission risk among serodiscordant couples: assessing the effects of combining prevention strategies.


Background: The number of strategies to prevent HIV transmission has increased following trials evaluating antiretroviral therapy (ART), pre-exposure prophylaxis (PrEP) and male circumcision. Serodiscordant couples need guidance on the effects of these strategies alone, and in combination with each other, on HIV transmission.

Methods: We estimated the sexual risk of HIV transmission over 1-year and 10-year periods among male-male and male-female serodiscordant couples. We assumed the following reductions in transmission: 80% from consistent condom use; 54% from circumcision in the negative male partner of a heterosexual couple; 73% from circumcision in the negative partner of a male-male couple; 71% from PrEP in heterosexual couples; 44% from PrEP in male-male couples; and 96% from ART use by the HIV-infected partner.

Findings: For couples using any single prevention strategy, a substantial cumulative risk of HIV transmission remained. For a male-female couple using only condoms, estimated risk over 10 years was 11%; for a male-male couple using only condoms, estimated risk was 76%. ART use by the HIV-infected partner was the most effective single strategy in reducing risk; among male-male couples, adding consistent condom use was necessary to keep the 10-year risk below 10%.

Conclusion: Focusing on 1-year and longer term transmission probabilities gives couples a better understanding of risk than those illustrated by data for a single sexual act. Long-term transmission probabilities to the negative partner in serodiscordant couples can be high, though these can be substantially reduced with the strategic use of preventive methods, especially those that include ART.

Abstract access

Editor's notes: This mathematical modelling study by Lasry et al, seeks to estimate how existing prevention strategies might be used by serodiscordant couples in hetero- and homosexual relationships to obtain optimal reduction in risk of HIV transmission. They illustrate that even modest transmission probabilities for a given type of sex act can accumulate into substantial risk over time. While it is recognised that anal sex poses a high risk for HIV transmission, the projections in this study show the extent of accumulated risk. The study importantly shows that condom use alone, provides quite inadequate protection over time. Not surprisingly given recent evidence, antiretroviral therapy (ART) had the most substantial protective effect. But condom use is an important adjunct to minimise long-term transmission risk. This is not only, but especially with consistent anal sex as in male homosexual, serodiscordant couples. The most important take-home finding of this study in influencing prevention messaging, is its quantitative illustration that combination prevention is the key to effective HIV prevention.

Methods of using real-time social media technologies for detection and remote monitoring of HIV outcomes.

Objective: Recent availability of "big data" might be used to study whether and how sexual risk behaviors are communicated on real-time social networking sites and how data might inform HIV prevention and detection. **This study seeks to establish methods of using real-time social networking data for HIV prevention by assessing 1) whether geolocated conversations about HIV risk behaviors can be extracted from social networking data, 2) the prevalence and content of these conversations, and 3) the feasibility of using HIV risk-related real-time social media conversations as a method to detect HIV outcomes.**

Methods: In 2012, tweets (N=553 186 061) were collected online and filtered to include those with HIV risk-related keywords (e.g., sexual behaviors and drug use). Data were merged with AIDSVU data on HIV cases. Negative binomial regressions assessed the relationship between HIV risk tweeting and prevalence by county, controlling for socioeconomic status measures.

Results: **Over 9 800 geolocated tweets were extracted and used to create a map displaying the geographical location of HIV-related tweets. There was a significant positive relationship (p<.01) between HIV-related tweets and HIV cases.**

Conclusion: Results suggest the feasibility of using social networking data as a method for evaluating and detecting Human immunodeficiency virus (HIV) risk behaviors and outcomes.

Abstract access

**Editor’s notes:** The concept of Big Data refers to data sets so large that they are almost or actually impossible to analyse or manage. Methods for harnessing big data sets, such as from social network sites online, are being developed for a variety of uses. These include understanding consumers for the purposes of building creative product marketing campaigns to predicting outbreaks of influenza. This paper examined the potential for using big data from Twitter to compare with areas of high HIV prevalence in the United States, to predict areas of increasing new HIV infections. There are several limitations for the method used in this paper. However, the idea presents an interesting concept. This study was conducted in a developed country, and while computers may not be readily available in resource limited settings, mobile phones are in use in most populations around the world. With mobile technology becoming increasingly sophisticated, and online social networking becoming more common, even in resource limited settings, this may be a strategy worth considering. It could be used in high HIV incidence networks within countries with high rates of HIV, especially in generalised epidemics. Clearly, this method will require additional research, validation and time to develop, but it could present a novel approach for estimating incidence without expensive testing.

2. **Prevent HIV among drug users**

Access to harm reduction programs among persons who inject drugs: findings from a respondent-driven sampling survey in Tehran, Iran.


Background: Over the past two decades, drug injection-related risk behaviors have been the major drivers of the HIV epidemic in Iran. This study assesses the access of people who injected drugs...
(PWID) to harm reduction services (needle-exchange programs [NEP] and methadone maintenance treatment [MMT]) in Tehran, Iran in 2007, almost five years after the large-scale implementation of these programs.

Methods: 572 consenting PWID (>18 years old, ever injected in the past month, lived in Tehran or its suburbs) were recruited (24 seeds) into a sero-behavioral survey using respondent-driven sampling method. Participants completed a face-to-face interview about HIV-related risk behaviors and access to harm reduction services. We calculated adjusted population estimates using RDSAT.

Results: Overall, 99.2% of the participants were male, 41.6% aged between 30 and 39 years old, 55.4% lived alone in the past year, 83.2% were ever incarcerated, and 88.8% lived in the southern areas of Tehran. In terms of “awareness” and “use” of services among PWID, 62.8% and 54.8% reported for NEP (respectively) and 19.7% and 9.1% for drug treatment services (respectively). PWID who lived in Northwest and South-central Tehran were more likely to be aware (85.0% and 82.8%, respectively) of one or more services than PWID who lived elsewhere. Similarly, PWID who lived with friends were more likely to be aware of (88.6%) and use (85.9%) services (vs. other living partners). Overall, 11% of the participants were aware of but had not used any harm reduction services.

Conclusions: Despite a relatively high level of access to NEP among PWID in Tehran, a sizable fraction of the population remains without access to other services five years after their implementation. The use of harm reduction may be affected by certain PWID characteristics (e.g., living partners and geographical location). Ongoing surveillance activities are necessary to track change in access over time.

Abstract access

Editor’s notes: This paper reports on findings of sero-behavioural survey among people who inject drugs (PWID) conducted in Tehran, The Islamic Republic of Iran. The paper provides a comprehensive description of harm reduction services available in Iran consisting of needle syringe programmes (NSP), methadone maintenance and drug detoxification services and summarises uptake of services among the study sample. The study describes the social-demographic characteristics of PWID, and finds that as elsewhere the majority of PWID recruited into the study are male aged under 40 years. This is similar to the age of PWID in western Europe but older than in eastern Europe (Platt, Jolley, Hope et al June 2013) The study suggests high rates of imprisonment and low rates of HIV testing. The majority of the sample had never been tested for HIV, whereas in western Europe over 90% of PWID participating in studies report experience of HIV testing. The study suggests that a high proportion of PWID are using NSPs at 55% (RDS adjusted estimate). This is high compared to estimates from Europe where proportions of PWID accessing NSPs ranges between 1% in Georgia, 4% in France to much higher in Finland at 81% and 68% in Lithuania. Low uptake of HIV testing but high uptake of NSP suggest that providing HIV testing at NSP sites would be a good way of increasing HIV testing. The study found that uptake of harm reduction programmes is associated with living partners. This suggests there might be a role for ‘secondary distribution’ of injecting equipment via partners or social networks to engage people currently not using services and to increase the use of harm reduction services.
3. 15 million accessing treatment

Delayed switch of antiretroviral therapy after virologic failure associated with elevated mortality among HIV-infected adults in Africa.


Objective: Routine monitoring of plasma HIV RNA among HIV-infected patients on antiretroviral therapy (ART) is unavailable in many resource-limited settings. Alternative monitoring approaches correlate poorly with virologic failure and can substantially delay switch to second-line therapy. We evaluated the impact of delayed switch on mortality among patients with virologic failure in Africa.

Design: A cohort.

Methods: We examined patients with confirmed virologic failure on first-line nonnucleoside reverse transcriptase inhibitor (NNRTI)-based regimens from four cohorts with serial HIV RNA monitoring in Uganda and South Africa. Marginal structural models aimed to estimate the effect of delayed switch on mortality in a hypothetical trial in which switch time was randomly assigned. Inverse probability weights adjusted for measured confounders including time-updated CD4 cell count and HIV RNA.

Results: Among 823 patients with confirmed virologic failure, the cumulative incidence of switch 180 days after failure was 30% [95% confidence interval (95% CI 27-33]. The majority of patients (74%) had not failed immunologically (as defined by WHO criteria) by the time of virologic failure. Adjusted mortality was higher for individuals who remained on first-line therapy than for those who had switched [odds ratio (OR) 2.1, 95% CI 1.1-4.2]. Among those without immunologic failure, the relative harm of failure to switch was similar (OR 2.4; 95% CI 0.99-5.8) to that of the entire cohort, although of borderline statistical significance.

Conclusion: Among HIV-infected patients with confirmed virologic failure on first-line ART, remaining on first-line therapy led to an increase in mortality relative to switching. Our results suggest that detection and response to confirmed virologic failure could decrease mortality.

Abstract access

Editor’s notes: The World Health Organization recommends scaling up access to routine viral load monitoring. This will enable healthcare workers to detect non-adherence and virologic failure earlier and to intervene to re-establish virologic control. This could be either on first-line antiretroviral therapy (ART) or by switching to second-line ART. If successful, this should limit the duration of viraemia, thereby limiting accumulation of resistance mutations and conserving future treatment options. The effect of viral load monitoring on mortality is less certain. To date, no randomised controlled trial has demonstrated a survival benefit of viral load monitoring over and above CD4 count monitoring. This may be due to study design - short follow-up time and intensive adherence support meant that few people experienced virologic failure. Previous observational studies described lower mortality in a South African cohort monitored using viral load monitoring as compared to a Malawian and Zambian cohort using CD4 count monitoring. However, subsequent mathematical modelling indicated that viral load monitoring only accounted for a small proportion of this difference. The rest was due to differences in resources, infrastructure and other unmeasured confounders.

This study explored the impact on mortality of delayed switching following confirmed virologic failure. Among 7 975 people initiated on ART between 2002-2011, some 823 experienced confirmed virologic
failure. As described by others, even in the context of routine viral load monitoring and access to second-line ART, marked delays in switching occur. The cumulative incidence of switching to second-line ART within six months of confirmed failure in this study was only 30%. Some of these ‘delays’ may have been due to the study definition of virologic failure. A lower viral load threshold was used in this study than was likely to have been used in the clinical guidelines. Delays could also have been due to healthcare system factors such as delayed turn-around-time for results or difficulties in recalling people. However, healthcare worker factors, such as delayed switching to address adherence barriers or to avoid drug interactions, particularly with treatment for tuberculosis, are also likely to also have played a part. Regardless of the reasons for delays, after adjusting for measured confounders, mortality was higher for people who experienced delayed switching. Longer delay was associated with higher probability of death.

This study indicates that viral load monitoring alone may not be sufficient to reduce mortality. A greater understanding of the reasons for delays, together with innovative ways to ensure virologic failure is detected and managed in an effective, timely manner, is needed.

Diagnostic accuracy of the WHO clinical staging system for defining eligibility for ART in sub-Saharan Africa: a systematic review and meta-analysis.


Introduction: The World Health Organization (WHO) recommends that HIV-positive adults with CD4 count ≤500 cells/mm³ initiate antiretroviral therapy (ART). In many countries of sub-Saharan Africa, CD4 count is not widely available or consistently used and instead the WHO clinical staging system is used to determine ART eligibility. However, concerns have been raised regarding its discriminatory ability to identify patients eligible to start ART. We therefore reviewed the accuracy of WHO stage 3 or 4 assessment in identifying ART eligibility according to CD4 count thresholds for ART initiation.

Methods: We systematically searched PubMed and Global Health databases and conference abstracts using a comprehensive strategy for studies that compared the Results of WHO clinical staging with CD4 count thresholds. Studies performed in sub-Saharan Africa and published in English between 1998 and 2013 were eligible for inclusion according to our predefined study protocol. Two authors independently extracted data and assessed methodological quality and risk of bias using the Quality Assessment Tool for Diagnostic Accuracy Studies (QUADAS-2) tool. Summary estimates of sensitivity and specificity were derived for each CD4 count threshold and hierarchical summary receiver operator characteristic curves were plotted.

Results: Fifteen studies met the inclusion criteria, including 25 032 participants from 14 countries. Most studies assessed individuals attending ART clinics prior to treatment initiation. WHO clinical stage 3 or 4 disease had a sensitivity of 60% (95% CI: 45-73%, Q=914.26, p<0.001) and specificity of 73% (95% CI: 60-83%, Q=1439.43, p<0.001) for a CD4 threshold of ≤200 cells/mm³ (11 studies); sensitivity and specificity for a threshold of CD4 count ≤350 cells/mm³ were 45% (95% CI: 26-66%, Q=1607.31, p<0.001) and 85% (95% CI: 69-93%, Q=896.70, p<0.001), respectively (six studies). For the threshold of CD4 count ≤500 cells/mm³ sensitivity was 14% (95% CI: 13-15%) and specificity was 95% (95% CI: 94-96%) (one study).

Conclusions: When used for individual treatment decisions, WHO clinical staging misses a high proportion of individuals who are ART eligible by CD4 count, with sensitivity falling as CD4 count criteria rises. Access to accurate, accessible, robust and affordable CD4 count testing...
methods will be a pressing need for as long as ART initiation decisions are based on criteria other than seropositivity.

Abstract    Full-text [free] access

Editor’s notes: This study highlights the major shortcomings of WHO clinical staging when identifying antiretroviral therapy (ART) eligible individuals, with decreasing sensitivity of clinical staging for eligibility at higher CD4 thresholds. There remains limited access to CD4 count testing in many settings in sub-Saharan Africa. The individual and public health benefit of earlier ART initiation will not be achieved unless strategies other than WHO clinical staging are implemented. Access to affordable, quality assured CD4 count testing in all ART initiation clinics may never be feasible in the most resource-constrained settings. Universal treatment, removing the need for CD4 count testing, may be the way to ensure that eligible individuals are started on ART in a timely way.

Decentralization of HIV care and treatment services in Central Province, Kenya.


Background: Since 2006, the government of Kenya began decentralizing HIV care from secondary health facilities (SHF) to an expanded network including primary health facilities (PHF). We evaluated the impact of this strategy on enrollment, care, and outcomes among adult patients in Central Province, Kenya from 2006 to 2010.

Methods: We analyzed electronic patient-level data for 26 690 patients at 15 SHF and 22 PHF. Enrollment, patient and facility characteristics, and patterns in CD4+ testing, WHO staging, and ART initiation were compared between SHF and PHF. Survival analysis was used to estimate cumulative death and loss to follow-up (LTF) rates in PHF and SHF. Multivariate competing risks regression and Cox proportional hazards models were constructed to identify correlates of LTF and death.

Results: Enrollment in PHF increased mainly between 2007 and 2009, representing 5% and 25% of all new enrollments, respectively. CD4+ test provision and WHO staging, time to ART initiation, and CD4+ count at ART initiation were for the most part similar between PHF and SHF. In multivariate analyses, pre-ART patients enrolled in PHF had a lower risk of LTF than those enrolled in SHF (SHR=0.77, 95% CI: 0.61-0.96). No differences in risk of death among pre-ART patients, or in LTF or death among ART patients were observed.

Conclusion: Enrollment at PHF increased substantially during the period; death rates were comparable between PHF and SHF, while LTF among pre-ART patients was lower at PHF. This suggests that decentralization can be a successful strategy for expanding HIV care.

Abstract access

Editor’s notes: As with many other countries in sub-Saharan Africa, Kenya has chosen the strategy of decentralisation of HIV services to peripheral health centres, to close the treatment gap.

The authors of this paper compared enrolment, people’ characteristics, and outcomes among nearly 27 000 people in HIV care at primary and secondary health facilities between 2006 and 2010. Over this period, the proportion of people living with HIV enrolled in care at primary health facilities increased substantially. People at primary health facilities had a somewhat healthier profile. This was
possibly due to self-selection where sicker people refer themselves to secondary health facilities. No differences in mortality and loss to follow-up among people on antiretroviral therapy (ART) were observed between primary and secondary health facilities. Retention in care among people not yet on ART can be particularly challenging. So the finding that people in primary health facilities experienced lower loss to follow-up rates compared to people using secondary health facilities is useful evidence in support of decentralised care.

Decentralisation of care sometimes raises concerns that the quality of care may be less good when delivered by less specialised staff. This study compared quality of services such as assessment of people for ART eligibility and time to ART initiation. The authors found similar quality of services at primary and secondary health facilities. Interestingly people at primary health facilities were initiated earlier on ART after HIV diagnosis, possibly due to more frequent assessment of ART eligibility at these centres. This large study is a useful addition to the evidence base supporting decentralised HIV care, with no evidence of loss of quality.

4. Avoid TB deaths

Interventions to improve delivery of isoniazid preventive therapy: an overview of systematic reviews.


Background: Uptake of isoniazid preventive therapy (IPT) to prevent tuberculosis has been poor, particularly in the highest risk populations. Interventions to improve IPT delivery could promote implementation. The large number of existing systematic reviews on treatment adherence has made drawing conclusions a challenge. To provide decision makers with the evidence they need, we performed an overview of systematic reviews to compare different organizational interventions to improve IPT delivery as measured by treatment completion among those at highest risk for the development of TB disease, namely child contacts or HIV-infected individuals.

Methods: We searched the Cochrane Database of Systematic Reviews, the Database of Abstracts of Reviews of Effects (DARE), and MEDLINE up to August 15, 2012. Two authors used a standardized data extraction form and the AMSTAR instrument to independently assess each review.

Results: Six reviews met inclusion criteria. Interventions included changes in the setting/site of IPT delivery, use of quality monitoring mechanisms (e.g., directly observed therapy), IPT delivery integration into other healthcare services, and use of lay health workers. Most reviews reported a combination of outcomes related to IPT adherence and treatment completion rate but without a baseline or comparison rate. Generally, we found limited evidence to demonstrate that the studied interventions improved treatment completion.

Conclusions: While most of the interventions were not shown to improve IPT completion, integration of tuberculosis and HIV services yielded high treatment completion rates in some settings. The lack of data from high burden TB settings limits applicability. Further research to assess different IPT delivery interventions, including those that address barriers to care in at-risk populations, is urgently needed to identify the most effective practices for IPT delivery and TB control in high TB burden settings.
Editor’s notes: Isoniazid preventive therapy (IPT) is a key component of the “3 Is” strategy to reduce tuberculosis among people living with HIV. Despite evidence of efficacy, initiation of IPT among eligible people in HIV care programmes has been disappointing. When IPT has been delivered as a stand-alone activity, treatment completion has often been poor. This overview of systematic reviews brings together evidence concerning organisational programmes to improve IPT delivery, using treatment completion as the main outcome. Three of the six included reviews, specifically included HIV-positive people.

When IPT delivery was integrated into other services, such as HIV care, good IPT completion rates were reported. A common weakness in the studies reviewed, was the lack of a suitable comparison group. This made it difficult to be sure that the good outcomes were due to the service integration. HIV This Month reported in June 2014 a trial from South Africa, showing that IPT reduces TB incidence among people taking antiretroviral therapy. Viewed together, these studies provide additional evidence supporting IPT delivery as part of the package of care for people in HIV care. More research is needed to guide implementers on how to deliver TB preventive therapy most effectively for people living with HIV.

Cryptococcal meningitis management in Tanzania with strict schedule of serial lumbar punctures using intravenous tubing sets: an operational research study.


Background: Cryptococcal meningitis (CM) has a mortality rate of approximately 70% among HIV-infected adults in low-income countries. Controlling intracranial pressure (ICP) is essential in CM, but it is difficult in low-income countries because manometers and practical ICP management protocols are lacking.

Methods: As part of a continuous quality improvement project, our Tanzanian hospital initiated a new protocol for ICP management for CM. All adult inpatients with CM are included in a prospective patient registry. At the time of analysis, this registry included data from 2 years before the initiation of this new ICP management protocol and for a 9-month period after. ICP was measured at baseline and at days 3, 7, and 14 by both manometer and intravenous (IV) tubing set. All patients were given IV fluconazole according to Tanzanian treatment guidelines and were followed until 30 days after admission.

Results: Among adult inpatients with CM, 32 of 35 patients (91%) had elevated ICP on admission. Cerebrospinal fluid pressure measurements using the improvised IV tubing set demonstrated excellent agreement ($r = 0.96$) with manometer measurements. Compared with historical controls, the new ICP management protocol was associated with a significant reduction in 30-day mortality (16/35 [46%] vs. 48/64 [75%] in historical controls; hazard ratio = 2.1 [95% CI: 1.1 to 3.8]; $P = 0.018$).

Conclusions: Increased ICP is almost universal among HIV-infected adults admitted with CM in Tanzania. Intensive ICP management with a strict schedule of serial lumbar punctures reduced in-hospital mortality compared with historical controls. ICP measurement with IV tubing sets may be a good alternative in resource-limited health facilities where manometers are not available.
**Editor’s notes:** Cryptococcal meningitis remains an important cause of morbidity and mortality among people with advanced HIV disease. Management is difficult in resource-limited settings. This is in part because optimal drug treatments are often not accessible, but also because of increased intracranial pressure, which may require repeated lumbar puncture. This should be done ideally using specialist equipment to measure intracranial pressure. This operational research study from United Republic of Tanzania illustrates the effectiveness of a standardised management protocol to manage intracranial pressure, using equipment which is widely available in resource-constrained settings. The simplified equipment produced pressure measurements which agreed well with measures from the “gold standard” manometer, and people managed according to this protocol experienced lower mortality than historical controls. However, mortality was still higher than would be expected in industrialised countries, illustrating the need for improved access to more effective antifungal drugs.

5. Close the resource gap

Scaling up integrated prevention campaigns for global health: costs and cost-effectiveness in 70 countries.


Objective: This study estimated the health impact, cost and cost-effectiveness of an integrated prevention campaign (IPC) focused on diarrhoea, malaria and HIV in 70 countries ranked by per capita disability-adjusted life-year (DALY) burden for the three diseases.

Methods: We constructed a deterministic cost-effectiveness model portraying an IPC combining counselling and testing, cotrimoxazole prophylaxis, referral to treatment and condom distribution for HIV prevention; bed nets for malaria prevention; and provision of household water filters for diarrhoea prevention. We developed a mix of empirical and modelled cost and health impact estimates applied to all 70 countries. One-way, multiway and scenario sensitivity analyses were conducted to document the strength of our findings. We used a healthcare payer’s perspective, discounted costs and DALYs at 3% per year and denominated cost in 2012 US dollars.

Primary and secondary outcomes: The primary outcome was cost-effectiveness expressed as net cost per DALY averted. Other outcomes included cost of the IPC; net IPC costs adjusted for averted and additional medical costs and DALYs averted.

Results: Implementation of the IPC in the 10 most cost-effective countries at 15% population coverage would cost US$583 million over 3 years (adjusted costs of US$398 million), averting 8.0 million DALYs. Extending IPC programmes to all 70 of the identified high-burden countries at 15% coverage would cost an adjusted US$51.3 billion and avert 78.7 million DALYs. Incremental cost-effectiveness ranged from US$49 per DALY averted for the 10 countries with the most favourable cost-effectiveness to US$119, US$181, US$335, US$1 692 and US$8 340 per DALY averted as each successive group of 10 countries is added ordered by decreasing cost-effectiveness.

Conclusions: IPC appears cost-effective in many settings, and has the potential to substantially reduce the burden of disease in resource-poor countries. This study increases confidence that IPC can be an important new approach for enhancing global health.

Abstract Full-text [free] access
Editor’s notes: Increasingly governments and policy makers are seeking to identify how to invest resources most effectively, to achieve multiple health and development outcomes. This paper presents a cost-effectiveness analysis of an integrated campaign to prevent diarrhoea, malaria and HIV.

They developed a model to estimate the cost per disability adjusted life year (DALY) averted by this intervention, across 70 countries with high disease burden, assuming 15% coverage. The authors categorise countries by income level and their opportunity index (i.e. the opportunity to avert DALYs by having a high disease burden). The findings suggest that an integrated prevention campaign (IPC) could cost as little as US$7 per DALY averted in Guinea-Bissau, a low income, high opportunity country. As would be expected, the contribution of the different IPC components varied by country, depending on their relative disease burdens. This suggests that further focusing of activities within countries may further improve efficiency.

The model was also used to consider potential roll out strategies across counties. For this, countries were grouped into blocks of 10, and ordered with increasing incremental-cost effectiveness. The authors suggest that reaching the top 40 countries with IPC, even at just 15% coverage, could achieve far greater health benefits, with a substantially lower budget, than requested under PEPFAR for antiretroviral therapy alone.

This paper provides further evidence of the need for a more integrated approach to improve population health across disease areas.

6. Eliminate gender inequalities

Widow cleansing and inheritance among the Luo in Kenya: the need for additional women-centred HIV prevention options.


Introduction: The customs of widow cleansing and widow inheritance are practiced in several communities throughout sub-Saharan Africa. In the Nyanza Province of Kenya, according to tradition, Luo widows are expected to engage in sexual intercourse with a “cleanser,” without the use of a condom, in order to remove the impurity ascribed to her after her husband’s death. Luo couples, including widows, are also expected to engage in sex preceding specific agricultural activities, building homes, funerals, weddings, and other significant cultural and social events. Widows who are inherited for the purpose of fulfilling cultural obligation have a higher prevalence of HIV than those who remain un-inherited or are inherited for the purpose of companionship.

Methods: As part of a larger descriptive qualitative study to inform study procedures for FEM-PrEP, an HIV prevention pre-exposure prophylaxis clinical trial, we conducted 15 semi-structured interviews (SSIs) with widows, 15 SSIs with inheritors, and four focus group discussions with widows in the Bondo and Rarieda districts in Nyanza Province to explore the HIV risk context within widow cleansing and inheritance practices. Thematic qualitative analysis was used to analyze the data.

Results: The majority of widows reported in the demographic questionnaire being inherited, and most widows in the SSIs described participating in the cleansing ritual. We identified two main themes related to HIV prevention within the context of widow cleansing and inheritance: 1) widows must
balance limiting their risk for HIV infection with meeting cultural expectations and ensuring that their livelihood needs are met, and 2) sexual abstinence undermines cultural expectations in widowhood while the use of condoms is deemed inappropriate in fulfilling culturally prescribed sexual rituals, and is often beyond the widow’s ability to negotiate.

Conclusions: Women-controlled HIV prevention methods such as antiretroviral-based oral pre-exposure prophylaxis, vaginal gels, and vaginal rings are needed for HIV-negative widows who engage in sexual rituals related to widowhood.

Abstract Full-text [free] access

Editor’s notes: This paper provides an in-depth insight into the practice of widow cleansing and its implications for widows’ vulnerability to contracting HIV. The paper describes the practice of widow cleansing by the Luo in Kenya. This entails the requirement for widows to have sexual intercourse with a non-relative of her deceased husband to “cleanse” the impurity she has acquired from the death of her husband. Following this practice widows are “inherited”, traditionally by an in-law but more recently by a professional inheritor who inherits widows for money. Relationships with professional inheritors commonly entail sexual intercourse and financial and emotional support for the widow. These relationships can be ended if not fulfilled to expectation. Alongside this, there are other expectations for widows to perform sexual intercourse with other men as part of ceremonies.

To understand the sexual risk-taking behaviours of Luo widows and inheritors, in-depth interviews and focus groups were conducted with widows and inheritors. This was part of a larger qualitative study during the FEM-PrEP trial. The findings revealed that widows were aware of their risk of HIV infection through cleansing and inheritance practices, which often entailed sexual intercourse without a condom. However, women’s concerns about this were outweighed by the need to fulfil cultural expectations to avoid being ostracised, and importantly to receive financial support. Whilst some women were able to use condoms with inheritors, this only occurred in new relationships or during menstruation or pregnancy. Widows and inheritors reported that condoms were rarely used during “cleansing” practices as the mixing of semen and vaginal fluids is essential to remove impurities.

Whilst this study reveals similar constraints on condom use for women in long-term relationships it highlights the additional complexity for Luo widows in relation to cleansing and inheritance practices. These practices legitimise multiple concurrent relationships and sex without a condom. Importantly, as a strongly embedded practice this gives widows limited options to use condoms or abstinence to prevent HIV infection. The authors suggest that Luo widows would benefit from access to biomedical HIV prevention methods, including PrEP and microbicides.

Community mobilization and empowerment of female sex workers in Karnataka state, south India: associations with HIV and sexually transmitted infection risk.


Objectives: We examined the impact of community mobilization (CM) on the empowerment, risk behaviors, and prevalence of HIV and sexually transmitted infection in female sex workers (FSWs) in Karnataka, India.

Methods: We conducted behavioral-biological surveys in 2008 and 2011 in 4 districts of Karnataka, India. We defined exposure to CM as low, medium (attended nongovernmental organization meeting or drop-in centre), or high (member of collective or peer group). We used regression analyses to
explore whether exposure to CM was associated with the preceding outcomes. Pathway analyses explored the degree to which effects could be attributable to CM.

Results: By the final survey, FSWs with high CM exposure were more likely to have been tested for HIV (adjusted odds ratio [AOR] = 25.13; 95% confidence interval [CI] = 13.07, 48.34) and to have used a condom at last sex with occasional clients (AOR = 4.74; 95% CI = 2.17, 10.37), repeat clients (AOR = 4.29; 95% CI = 2.24, 8.20), and regular partners (AOR = 2.80; 95% CI = 1.43, 5.45) than FSWs with low CM exposure. They were also less likely to be infected with gonorrhea or chlamydia (AOR = 0.53; 95% CI = 0.31, 0.87). Pathway analyses suggested CM acted above and beyond peer education; reduction in gonorrhea or chlamydia was attributable to CM.

Conclusions: CM is a central part of HIV prevention programming among FSWs, empowering them to better negotiate condom use and access services, as well as address other concerns in their lives.

Abstract access

Editor's notes: Community mobilization is a group empowerment strategy that focuses on the structural drivers of HIV transmission. Starting in 2003, the Karnataka Health Promotion Trust in India collaborated with female sex workers to recruit peer educators. This led to the creation of drop-in centres, distribution of presumptive treatment of gonorrhoea and chlamydia infection, and ultimately the formation of locally-sustained collectives and community-based organisations. In 2011, half of female sex workers in Karnataka were members of one of these groups. Members of these groups were more likely to have used condoms with their sex partners and were less likely to contract either gonorrhoea or chlamydia. The findings suggest that community mobilization may work because it is strongly associated with both collective (power with) and individual (power to) empowerment of sex workers. This is one of the first studies of community engagement to include biological outcomes for HIV and sexually transmitted infection, rather than self-reported measures of behaviour that may be susceptible to bias. The results suggest that such community empowerment approaches may form an integral part of HIV prevention programming in sex worker communities.

Women's land ownership and risk of HIV infection in Kenya.


Theory predicts that land ownership empowers women to avoid HIV acquisition by reducing their reliance on risky survival sex and enhancing their ability to negotiate safer sex. However, this prediction has not been tested empirically. Using a sample of 5,511 women working in the agricultural sector from the 1998, 2003 and 2008-09 Kenya Demographic and Health Surveys, we examined the relationship between women's land ownership and participation in transactional sex, multiple sexual partnerships and unprotected sex, and HIV infection status. We controlled for demographic characteristics and household wealth, using negative binomial and logistic regression models. Women's land ownership was associated with fewer sexual partners in the past year (incidence rate ratio, 0.98; 95% confidence interval [CI], 0.95-1.00) and lower likelihood of engaging in transactional sex (odds ratio [OR], 0.67; 95% CI: 0.46-0.99), indicators of reduced survival sex, but was not associated with unprotected sex with casual partners (OR, 0.64; 95% CI, 0.35-1.18) or with unprotected sex with any partner among women with high self-perceived HIV risk (OR, 1.02; 95% CI, 0.57-1.84), indicating no difference in safer sex negotiation. Land ownership was also associated with reduced HIV infection among women most likely to engage in survival sex, i.e., women not under the household headship of a husband (OR, 0.40; 95% CI, 0.18-0.89), but not among
women living in husband-headed households, for whom increased negotiation for safer sex would be more relevant (OR, 1.74; 95% CI, 0.92-3.29). These findings suggest that reinforcing women’s land rights may reduce reliance on survival sex and serve as a viable structural approach to HIV prevention, particularly for women not in a husband’s household, including unmarried women and female household heads.

Abstract access

Editor’s notes: A range of social and economic factors influence the degree to which individuals and communities are vulnerable to HIV infection. In some settings, a lack of land ownership has been shown to increase women’s risk of partner violence. This paper assessed whether women who own land have lower HIV risk. For single women or women in female-headed households, land ownership was associated with a reduced risk of HIV infection. Interestingly, lower HIV risk didn’t appear to be associated with an increased ability to negotiate safer sex practices, but rather arise from women’s reduced economic reliance on high-risk sexual partnerships. The findings also suggest that women’s own access to land had a greater influence on their HIV risk than household-level wealth, suggesting that household level wealth is not the same as wealth owned by women. Although the analysis is of cross-sectional data, and so causality cannot be established, the findings suggest that increasing women’s ownership of land may provide a structural mechanism to reduce women’s HIV vulnerability. This contributes to the increasing body of evidence that points to the potentially important role that economic empowerment programmes may play in helping to reduce women’s vulnerability to HIV.