

HIV This Week: what scientific journals said

Happy New Year and welcome to the 77th issue of **HIV This Week**! In this issue, we cover the following topics:

1. Stigma

- Stigma towards people living with HIV in the USA: time to move from studying stigma to learning how to foster resilience and solidarity
- Community popular opinion leaders and HIV-related stigma reduction in China

2. Treatment

- The details on DART you have been waiting to cite
- Foreigners have better antiretroviral treatment outcomes than citizens in Johannesburg – why?

3. Epidemiology

- Improving the accuracy of incidence assays: an uphill but essential battle to track progress
- Why has it taken so long to think about using repeated household-based surveys to estimate HIV incidence?

4. HIV testing

- The promise of home testing means different things in different settings
- Inaccurate HIV diagnoses in Cameroon: a wake-up call for national laboratory directors and programme managers everywhere

5. Paediatric ART

- Kids in resource-limited settings do just as well on antiretroviral treatment so let's get them started!
- CD4% and weight gain the first 6 months predict treatment outcomes in South African kids: new reference curves

6. Human rights

- Linking human rights obligations with structural interventions: how much Zimbabwe could do

7. Men who have sex with men

- HIV prevalence may be stabilizing in Bangkok but will current programming reverse the epidemic?

8. Basic science

- How using an Adenovirus vector in the STEP trial increased HIV risk: memory CD4 T cells with a mucosal homing phenotype got called up to fight and were easy prey

9. Implementation science

- What are the key research questions on the impact of HIV scale-up on health systems?

10. HIV-2

- HIV-1 rises and HIV-2 declines in rural Guinea-Bissau
- Why would patients with HIV-2 in Burkina Faso do worse on antiretroviral treatment when HIV-2 is less pathogenic than HIV-1?

11. Knowledge translation

- Where does the 'evidence-informed' bit best fit in policymaking and how can it be more influential?

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1. Stigma

Meta-analysis of health and demographic correlates of stigma towards people living with HIV.

Logie C, Gadalla TM. *AIDS Care*. 2009 2:742-53.

HIV-related stigma may negatively impact the health, quality of life, social support and well-being of people living with HIV (PLHIV). Previous studies have used diverse samples and a multitude of measurement instruments to examine demographic and health correlates of HIV-related stigma, highlighting the importance of synthesizing findings across different studies to gain a better understanding of these associations. This study examined the relationships between HIV-related stigma and a range of demographic, social, physical and health characteristics. A meta-analysis was conducted to assess the overall strength and direction of these relationships. **Twenty-four studies of PLHIV, conducted in North America** and published in peer-reviewed journals between January of 2000 and November of 2007, were examined and their findings integrated. The heterogeneity of reported results was also assessed and examined. Logie *et al's* review revealed substantial variability in the ways researchers measure participants' HIV-related stigma as well as their physical, emotional and mental health. In spite of this variability, **high stigma level was consistently and significantly associated with low social support ($r = -0.369$, $p < 0.0005$), poor physical health ($r = -0.324$, $p < 0.0005$), poor mental health ($r = -0.402$, $p < 0.0005$), age (-0.066 , $p < 0.05$) and income (-0.172 , $p < 0.005$).** These correlations were of a medium size, which would be recognized by the individual in daily life. **Health and mental health professionals** working with individuals and families affected by HIV **could benefit from an enhanced understanding of correlates of HIV-related stigma**, which will inform assessments, interventions, and treatment plans. The association between HIV-related stigma and physical health has potential implications for treatment, care and support for people at different stages of HIV infection. AIDS Service Organizations are also encouraged to integrate findings into HIV stigma interventions and social support programs. Additionally, HIV-related stigma scales should be developed and validated, so that future studies using them are able to report findings that are operationally and conceptually consistent.

Full text article:

<http://www.informaworld.com/smpp/content~db=all?content=10.1080/09540120802511877>

Editors' note: Drawing on data from 5600 individuals in 24 studies, this literature synthesis is the first to quantify the associations between HIV-related stigma and characteristics of people living with HIV. Five key variables were found to be significantly associated with high stigma levels: lack of social support, poor physical health, poor mental health, low income, and younger age. Effective interventions to address stigma operate on multiple levels and engage populations as diverse as policy makers, practitioners, communities, and people living with HIV. On a parallel track, it is high time to measure and better understand individual and collective strengths such as the resilience, resistance, solidarity, and empowerment that both help cope with stigma and reduce its prevalence.

HIV prevention intervention to reduce HIV-related stigma: evidence from China.

Li L, Liang LJ, Lin C, Wu Z, Rotheram-Borus MJ; the NIMH Collaborative HIV/STD Prevention Trial Group. *AIDS*. 2010 24:115-122.

The National Institute of Mental Health Collaborative HIV/Sexually Transmitted Disease Prevention Trial provided a unique opportunity to test whether, with the community-based diffusion of HIV/sexually transmitted disease prevention information and an elevated understanding of HIV, the level of stigmatizing attitudes toward people living with HIV in the community would be reduced. A total of **4510 market workers in Fuzhou, China**, participated in the study, and longitudinal analyses included study samples of 3785 participants in the 12-month follow-up and 3716 participants in the 24-month follow-up. The authors graphically examined the **change in HIV-related stigma indicators over time** between control and intervention groups using boxplot and kernel density estimation. A logistic regression analysis with proportional odds model was further

used to examine the intervention effect on HIV-related stigmatizing attitudes. Compared with no change over time for the control group, the intervention successfully **reduced the level of HIV-related stigmatizing attitudes among the target population at the 12-month follow-up**, and the effect **increased by two-fold** (with respect to odds ratios) at the **24-month follow-up**. The intervention demonstrated positive attitude changes associated with HIV-related stigma. These results show the importance of social norms, rather than simply individual behaviours, in developing and implementing stigma reduction campaigns.

Abstract only: <http://www.ncbi.nlm.nih.gov/pubmed/19926963>

Editors' note: This trial was designed to identify, recruit, train, and engage community popular opinion leaders to convey HIV-risk reduction messages to food vendors in the markets that were randomised to the intervention arm. The 'unintended' finding of stigma reduction in a trial designed to reduce HIV/STD incidence and risk behaviour is puzzling. It may be due to community mobilisation and the use of social networks to convey information. It does suggest that HIV prevention and stigma reduction initiatives should be integrated for maximum benefit.

2. Treatment

Routine versus clinically driven laboratory monitoring of HIV antiretroviral therapy in Africa (DART): a randomised non-inferiority trial.

DART Trial Team. The Lancet, Early Online Publication, 9 December 2009 [Epub ahead of print]

HIV antiretroviral therapy (ART) is often managed without routine laboratory monitoring in Africa; however, the effect of this approach is unknown. This trial investigated whether routine toxicity and efficacy monitoring of HIV-infected patients receiving antiretroviral therapy had an important long-term effect on clinical outcomes in Africa. In this **open, non-inferiority trial** in three centres in Uganda and one in Zimbabwe, **3321 symptomatic, antiretroviral therapy-naive, HIV-infected adults with CD4 counts less than 200 cells per μ L** starting antiretroviral therapy were randomly **assigned to laboratory and clinical monitoring (LCM; n=1659) or clinically driven monitoring (CDM; n=1662)** by a computer-generated list. Haematology, biochemistry, and CD4-cell counts were done every 12 weeks. **In the laboratory and clinical monitoring group, results were available to clinicians; in the clinically driven monitoring group, results (apart from CD4-cell count) could be requested if clinically indicated and grade 4 toxicities were available.** Participants switched to second-line antiretroviral therapy after new or recurrent WHO stage 4 events in both groups, or CD4 count less than 100 cells per μ L (laboratory and clinical monitoring only). Co-primary endpoints were new WHO stage 4 HIV events or death, and serious adverse events. Non-inferiority was defined as the upper 95% confidence limit for the hazard ratio (HR) for new WHO stage 4 events or death being no greater than 1.18. Analyses were by intention to treat. This study is registered, number ISRCTN13968779. Two participants assigned to clinically driven monitoring and three to laboratory and clinical monitoring were excluded from analyses. **5-year survival was 87% (95% CI 85-88) in the CDM group and 90% (88-91) in the LCM group**, and 122 (7%) and 112 (7%) participants, respectively, were lost to follow-up over median 4.9 years' follow-up. 459 (28%) participants receiving clinically driven monitoring versus 356 (21%) laboratory and clinical monitoring had a new WHO stage 4 event or died (6.94 [95% CI 6.33-7.60] vs 5.24 [4.72-5.81] per 100 person-years; **absolute difference 1.70 per 100 person-years** [0.87-2.54]; HR 1.31 [1.14-1.51]; $p=0.0001$). **Differences in disease progression occurred from the third year on antiretroviral therapy**, whereas **higher rates of switch to second-line treatment occurred in LCM from the second year**. 283 (17%) participants receiving clinically driven monitoring versus 260 (16%) LCM had a new serious adverse event (HR 1.12 [0.94-1.32]; $p=0.19$), with anaemia the most common (76 vs 61 cases). Antiretroviral therapy can be delivered safely without routine laboratory monitoring for toxic effects, but differences in disease progression suggest a role for monitoring of CD4-cell count from the second year of antiretroviral therapy to guide the switch to second-line treatment.

Full text article: [http://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(09\)62067-5/fulltext](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(09)62067-5/fulltext)

Editors' note: These findings, presented at the International AIDS Society conference in Cape Town in July 2009 are fully described here, complementing the excellent film produced by Tom Gibb (<http://www.youtube.com/MRCcomms#p/u/1/MSyFmbiR-Hc>). The results of this trial, designed to determine whether clinician monitoring of signs and symptoms without knowledge of CD4 count was not inferior to similar monitoring with knowledge of CD4 test results, suggest that once eligibility for antiretroviral treatment is determined, clinically driven monitoring holds the fort well for the first 2 years of treatment, freeing up resources and allowing extension of treatment access to more remote areas with no laboratory infrastructure.

Good treatment outcomes among foreigners receiving antiretroviral therapy in Johannesburg, South Africa.

McCarthy K, Chersich MF, Vearey J, Meyer-Rath G, Jaffer A, Simpwalo S, Venter WD. *Int J STD AIDS*. 2009 20:858-62.

Foreigners, including displaced persons, often have limited health-care access, especially to HIV services. Outcomes of antiretroviral therapy (ART) in South Africans and foreigners were compared at a Johannesburg non-governmental clinic. Records were reviewed of **1297 adults** enrolled between April 2004 and March 2007 (568 self-identified foreigners, 431 South Africans citizens and 298 with unknown origin). Compared with citizens, **foreigners had fewer hospital admissions** (39%, 90/303 versus 51%, 126/244; $P < 0.001$), **less missed appointments** for antiretroviral therapy initiation (20%, 39/200 versus 25%, 51/206; $P < 0.001$), **faster median time to antiretroviral therapy initiation** (14 versus 21 days, $P = 0.008$), **better retention in care** (88%, 325/369 versus 69%, 155/226; $P < 0.001$) and **lower mortality** (2.5%, 14/568 versus 10%, 44/431; $P < 0.001$) after 426 person-years. In logistic regression, after controlling for baseline CD4 count and tuberculosis status, **foreigners were 55% less likely to fail antiretroviral therapy than citizens** (95% CI = 0.23-0.87). These findings support United Nations High Commissioner for Refugees recommendations that antiretroviral therapy should not be withheld from displaced persons.

Abstract only: <http://ijsa.rsmjournals.com/cgi/content/abstract/20/12/858>

Editors' note: South Africa at the end of 2007 had the world's largest number of pending asylum applications and was second only to the United States of America in annual new asylum claims. The level of undocumented migrants is much higher. The findings from this study demonstrate that foreigners were about half as likely to fail antiretroviral treatment as citizens, despite having lower baseline median CD4 cell counts and being subject to significant hurdles in accessing and staying in care. This strongly supports the argument that foreigners should be included in the 'right to access antiretroviral treatment for all.

3. Epidemiology

Accuracy of serological assays for detection of recent infection with HIV and estimation of population incidence: a systematic review.

Guy R, Gold J, Calleja JM, Kim AA, Parekh B, Busch M, Rehle T, Hargrove J, Remis RS, Kaldor JM; WHO Working Group on HIV Incidence Assays. *Lancet Infect Dis*. 2009 9:747-59.

The authors systematically reviewed the accuracy of serological tests for recent infections with HIV that have become widely used for measuring population patterns incidence of HIV. Across 13 different assays, **sensitivity to detect recent infections ranged from 42-100% (median 89%)**. **Specificity for detecting established infections was between 49.5% and 100% (median 86.8%)** and was **higher for infections of durations longer than 1 year** (median 98%, range 31.5-100.0). For four different assays, comparisons were made between assay-derived population incidence estimates and a reference incidence estimate. **The median percentage difference between the assay-derived incidence and reference incidence was 26.0%**. Serological assays have reasonable sensitivity for the detection of recent infection with HIV, but are vulnerable to

misclassifying established infections as recent-potentially leading to biases in incidence estimates. This conclusion is highly qualified by the apparent absence of a standardised approach to assay evaluation. There is an urgent need for an internationally agreed framework for evaluating and comparing these tests.

Full text: [http://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(09\)70300-7/fulltext](http://www.thelancet.com/journals/laninf/article/PIIS1473-3099(09)70300-7/fulltext)

Editors' note: Determining HIV incidence directly by measuring seroconversion and thereby monitoring HIV transmission is key to both assessing the need for and establishing the effectiveness of HIV prevention programmes. This extensive review confirms that the development of reliable and valid tests to detect recent infection is a public health priority. To date virtually all the assays that have been developed involve subtype B virus (clade C is the most common worldwide) and have been plagued by false positive results due to longstanding infections or an increasing duration of antiretroviral treatment. Given that HIV incidence reduction is a foundation of both national and international HIV commitments, it is urgent that a standardised approach to assay validation be developed and implemented.

Estimates of HIV incidence from household-based prevalence surveys.

Hallett TB, Stover J, Mishra V, Ghys PD, Gregson S, Boerma T. AIDS. 2010 ;24:147-52.

This study set out to estimate HIV incidence in the general population in countries where there have been two recent household-based HIV prevalence surveys (the Dominican Republic, Mali, Niger, Tanzania, and Zambia). Hallett *et al* applied a validated method to estimate HIV incidence using HIV prevalence measurement in two surveys. The authors estimate **incidence among men and women aged 15-44 years** to be: **0.5/1000 person-years at risk in the Dominican Republic 2002-2007, 1.1/1000 in Mali 2001-2006, 0.6/1000 in Niger 2002-2006, 3.4/1000 in Tanzania 2004-2008, and 11.2/1000 in Zambia 2002-2007.** The groups most at risk in these epidemics are typically 15-24-year-old women and 25-39-year-old men. Incidence appears to have declined in recent years in all countries, but only significantly among men in the Dominican Republic and Tanzania and women in Zambia. **Using prevalence measurements to estimate incidence reveals the current level and age distribution of new infections and the trajectory of the HIV epidemic.** This information is more useful than prevalence data alone and should be used to help determine priorities for interventions.

Abstract: <http://www.ncbi.nlm.nih.gov/pubmed/19915447>

Editors' note: Why have we not been estimating HIV incidence from household surveys? This straightforward method of comparing current age cohorts with their representation in a previous survey includes adjustments for deaths and the numbers of people on treatment by age group. The gold standard, a cohort incidence study, is too expensive and the cohorts in question may not represent the national population anyway. Just as trends in HIV prevalence among pregnant women aged 15 to 24 years have been a proxy for HIV incidence, so too can this approach detect changes in HIV incidence, but at a variety of ages.

4. HIV testing

Home testing for HIV infection in resource-limited settings.

Ganguli I, Bassett IV, Dong KL, Walensky RP. Curr HIV/AIDS Rep. 2009;6:217-23.

Among an estimated 33 million individuals who are infected with HIV worldwide, only 10% are aware of their status. HIV testing is the cornerstone to preventing further transmission and to caring for those infected, particularly as access to treatment improves in resource-limited settings. However, efforts to expand testing through facilities-based testing have not achieved adequate testing coverage, prompting efforts to reach more individuals through strategies such as home-based HIV testing. **Home testing is showing promising early results in some high-prevalence, resource-limited settings.** This article reviews the mechanisms and literature to date of this door-to-door approach.

Editors' note: This review contrasts the literature on self-specimen collection and self-testing at home in the United States of America with 'counsellor-initiated home-based testing' in high HIV prevalence resource-limited settings. Those most likely to benefit from the latter may be the poor who have the lowest uptake of traditional, facility-based testing and counselling. Home-based testing in low- and middle-income settings may reach couples and families more efficiently than other strategies but individuals and the public will only benefit if there are strong links to effective HIV prevention, medical care, and psychosocial support for those who learn their test result.

Inaccurate diagnosis of HIV-1 group M and O is a key challenge for ongoing universal access to antiretroviral treatment and HIV prevention in Cameroon.

Aghokeng AF, Mpoudi-Ngole E, Dimodi H, Atem-Tambe A, Tongo M, Butel C, Delaporte E, Peeters M. PLoS One. 2009 ;4:e7702.

Increased access to HIV testing is essential in working towards universal access to HIV prevention and treatment in resource-limited countries. The authors evaluated currently used HIV diagnostic tests and algorithms in Cameroon for their ability to correctly identify HIV infections. They estimated sensitivity, specificity, and positive and negative predictive values of **5 rapid/simple tests**, of which 3 were used by the national program, and 2 fourth generation ELISAs. The reference panel included 500 locally collected samples; 187 HIV -1 M, 10 HIV-1 O, 259 HIV negative and 44 HIV indeterminate plasmas. **None of the 5 rapid assays and only 1 ELISA reached the current WHO/UNAIDS recommendations on performance of HIV tests of at least 99% sensitivity and 98% specificity.** Overall, sensitivities ranged between 94.1% and 100%, while specificities were 88.0% to 98.8%. The combination of all assays generated **up to 9% of samples with indeterminate HIV status**, because they reacted discordantly with at least one of the different tests. Including HIV indeterminate samples in test efficiency calculations significantly decreased specificities to a range from 77.9% to 98.0%. Finally, **two rapid assays failed to detect all HIV-1 group O variants tested, with one rapid test detecting only 2 out of 10 group O specimens.** In the era of antiretroviral therapy scaling-up in Africa, significant proportions of false positive but also false negative results are still observed with HIV screening tests commonly used in Africa, resulting in inadequate treatment and prevention strategies. Depending on tests or algorithms used, **up to 6% of HIV-1 M and 80% of HIV-1 O infected patients in Cameroon do not receive antiretroviral therapy and adequate counselling to prevent further transmission due to low sensitivities.** Also, the use of tests with low specificities could imply inclusion of up to 12% HIV negative people in antiretroviral therapy programs and increase budgets in addition to inconveniences caused to patients.

Full text: <http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0007702>

Editors' note: False-positive and false-negative HIV test results have negative implications for both individuals and programmes – all efforts must be made to minimise them. The first step is to evaluate assay performance using a serum panel from patients infected with subtypes that are circulating locally and the second step is instituting ongoing quality control. Inadequate sensitivity (ability to correctly identify presence of infection) and specificity (ability to correctly identify lack of infection) mean that infections are missed which can delay treatment or, on the other hand, that people who are not infected believe that they are, with personal and programmatic costs. When test kits are chosen by officials on the basis of lower price rather than performance efficacy, the results can be dire. This article should be essential reading for all national laboratory directors.

5. Paediatric ART

Effectiveness of paediatric antiretroviral therapy in resource-limited settings: a systematic review and meta-analysis.

Ciaranello AL, Chang Y, Margulis AV, Bernstein A, Bassett IV, Losina E, Walensky RP. Clin Infect Dis. 2009;49:1915-27.

Responses to antiretroviral therapy (ART) among human immunodeficiency virus (HIV)-infected children in resource-limited settings have recently been reported, but outcomes vary. The authors

sought to derive pooled estimates of the **12-month rate of virologic suppression (HIV RNA, <400 copies/mL) and gain in CD4 cell percentage (DeltaCD4%)** for children initiating antiretroviral therapy in resource-limited settings. Ciaranello *et al* conducted a systematic review and meta-analysis of published reports of HIV RNA and CD4 outcomes for treatment-naïve children aged 0-17 years old by means of the Medline, EMBASE (Excerpta Medica Database), and LILACS (Latin American and Caribbean Health Sciences Literature) electronic databases and the Cochrane Clinical Trials Register. Pooled estimates of the reported proportion with HIV RNA <400 copies/mL and DeltaCD4% after 12 months of antiretroviral therapy were derived using patient-level estimates and fixed- and random-effects models. To approximate intention-to-treat analyses, in sensitivity analyses children with missing 12-month data were assumed to have HIV RNA >400 copies/mL or DeltaCD4% of zero. In patient-level estimates **after 12 months of antiretroviral therapy, the pooled proportion with virologic suppression was 70%** (95% confidence interval [CI], 67%-73%); **the pooled DeltaCD4% was 13.7%** (95% CI, 11.8%-15.7%). Results from the fixed- and random-effects models were similar. In approximated intention-to-treat analyses, the pooled estimates decreased to **53% with virologic suppression** (95% CI, 50%-55%) and to a **DeltaCD4% of 8.5%** (95% CI, 5.5%-11.4%). Pooled estimates of reported virologic and immunologic benefits after 12 months of antiretroviral therapy among HIV-infected children in resource-limited settings are comparable with those observed among children in developed settings. Consistency in reporting on reasons for missing data will aid in the evaluation of antiretroviral therapy outcomes in resource-limited settings.

Full text:

http://www.journals.uchicago.edu/doi/abs/10.1086/648079?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%3dncl.nih.gov

Editors' note: Treatment outcomes for treatment-naïve children after 1 year are similar in resource-poor settings as they are in the United States of America and Europe, despite advanced stages of HIV disease at initiation of antiretroviral treatment, substantial barriers to service delivery, and predominantly non-nucleoside reverse transcriptase inhibitor (NNRTI)-based regimens. This is great news from this first study to provide pooled estimates of the virological suppression rate and change in CD4 percentage in children in countries with emerging or developing economies. These findings have particular importance for the estimated 90% of children living with HIV who reside in resource-limited settings and should spur on the movement to treat all children living with HIV.

Six-month gain in weight, height, and CD4 predict subsequent antiretroviral treatment responses in HIV-infected South African children.

Yotebieng M, Van Rie A, Moultrie H, Meyers T. AIDS. 2010 24:139-46.

The aim of the study was to construct percentile curves for 6-month gain in weight, height, CD4 cell count, and CD4 percentage (CD4%) in children initiating antiretroviral therapy, and to assess the association between lower percentiles and subsequent antiretroviral therapy responses. A cohort of **1394 HIV-infected children** initiating antiretroviral therapy between April 2004 and March 2008, Johannesburg, South Africa were enrolled. The generalized additive model for location, scale, and shape was used to **construct percentile curves for 6-month gain in weight, height, CD4 cell count, and CD4%**. Cox proportional models were used to assess the association between lower percentiles of each distribution and death, virological suppression, and treatment failure between 6 to 36 months post-antiretroviral therapy initiation. **Lower percentiles for gain in weight, CD4, and CD4% count after 6 months of antiretroviral therapy**, but not height, were **associated with poor subsequent treatment outcomes independent of baseline characteristics, with increasing strength of association as percentiles decreased**. Age-specific 6-month post-antiretroviral therapy weight gain in this cohort was substantially higher compared with 6-month weight gain in non-HIV-infected American children of the Fels Institute cohort and the attained weight-for-age at 6 months post- antiretroviral therapy plotted on WHO weight-for-age growth charts were not associated with subsequent treatment outcomes. Gain in CD4% in the first 6 months of antiretroviral therapy was the best predictor of poor subsequent

antiretroviral therapy outcomes. In areas with limited access to CD4%, **weight gain post-antiretroviral therapy using these newly developed reference distributions for HIV-infected children on antiretroviral therapy is a good alternative to CD4%**, and clearly superior to the commonly used 'Road-to-Health' weight-for-age charts.

Abstract only: <http://www.ncbi.nlm.nih.gov/pubmed/19940744>

Editors' note: A third of children vertically infected do not survive to their first birthday and more than half die before age 2. When children start antiretroviral treatment, it is important to monitor their clinical improvement to assess whether they are benefitting. This innovative study developed HIV-specific weight gain reference curves that can be used by health workers in settings without CD4 percentage laboratory tests to identify which children on treatment are likely to be virologically suppressed and which ones are at higher risk for treatment failure and subsequent death. These reference curves should be tested in other settings and adjusted as necessary to develop international weight gain reference curves for children starting antiretroviral treatment.

6. Human rights

Structural barriers and human rights related to HIV prevention and treatment in Zimbabwe.

Amon JJ, Kasambala T. Glob Public Health. 2009;4:528-45.

There has long been recognition that **individual risk factors can only partially explain vulnerability to HIV infection**, and that a broader range of socioeconomic, cultural and political factors must be taken into account. More recently this understanding has been applied to addressing obstacles to accessing HIV treatment. Yet, while structural interventions aimed at contextual factors related to HIV prevention and treatment have been shown to be effective, they have not been widely implemented. Using the situation of Zimbabwe as an example, Amon *et al* present an illustration of **how contextual barriers can be understood in human rights terms**, and **how using a human rights analysis can specifically help define 'structural-rights' interventions** and compel their implementation.

Abstract: <http://www.ncbi.nlm.nih.gov/pubmed/19326281>

Editor's note: In linking human rights obligations and structural-rights interventions, this paper considers four categories of global human rights concerns: the right to earn a livelihood and own property; the right to freedom of expression, assembly, and information; the right to freedom from gender-based and sexual violence; and the right to the progressive realisation of health. Using the situation of Zimbabwe as an illustration, the paper presents a list of structural-rights interventions linked to goals addressing each of these human rights concerns. This analytic framework explicitly links interventions to redress societal inequities, reduce vulnerability to HIV, and expand access to treatment with state obligations under national and international law. It reinforces the role of governments to address structural barriers and human rights abuses as part of their broader mission of public health.

7. Men who have sex with men

Trends in HIV Prevalence, Estimated HIV Incidence, and Risk Behaviour Among Men Who Have Sex With Men in Bangkok, Thailand, 2003-2007.

van Griensven F, Varangrat A, Wimonstate W, Tanpradech S, Kladsawad K, Chemnasiri T, Suksripanich O, Phanuphak P, Mock P, Kanggarnrua K, McNicholl J, Pliapat T. J Acquir Immune Defic Syndr. 2009 No. [Epub ahead of print]

Men who have sex with men (MSM) continue to be at high risk for HIV infection. Here the authors evaluate trends in HIV prevalence, estimated HIV incidence, and risk behaviour among MSM in Bangkok, Thailand. Between 2003 and 2007, 3 biennial cross-sectional HIV prevalence assessments were conducted among men who have sex with men in Bangkok, Thailand, using venue-day-time sampling. **Oral fluid** was tested for HIV infection; **demographic and behavioural**

data were self-collected using hand-held computers. Estimates of annual HIV incidence in young men who have sex with men were derived as follows: (number of HIV infections/sum of [current age-age at start of anal intercourse]) x 100). Logistic and Poisson regression was used to evaluate trends in HIV prevalence, estimated HIV incidence, and risk behaviour. **The overall HIV prevalence increased from 17.3% in 2003 to 28.3% in 2005 to 30.8% in 2007 (P < 0.001 for trend).** The **estimated HIV incidence among young men who have sex with men increased from 4.1% in 2003 to 6.4% in 2005, to 7.7% in 2007 (P < 0.02 for trend).** The increase in HIV prevalence from 2005 to 2007 was not statistically significant. The **proportion of men reporting anal sex and casual or steady male sex partners in the past 3 months significantly decreased,** whereas the **proportion reporting drug use and drug use during sex significantly increased.** No increase was observed in the proportion of men reporting consistent condom use. These data suggest that after a strong increase from 2003 to 2005, the HIV prevalence among men who have sex with men in Bangkok may have begun to stabilize. Given the continuing high levels of risk behaviour and the estimated high HIV incidence in young MSM, additional HIV preventive interventions are necessary.

Abstract: <http://www.ncbi.nlm.nih.gov/pubmed/19901844>

Editors' note: The high HIV prevalence in Bangkok among men who have sex with men is part of the global phenomenon of resurgent or newly described HIV epidemics among men who have sex with men around the world. The encouraging signs of a possible epidemic plateau should not distract from the need to intensify efforts towards universal access to services and prevention interventions for this key population. It is clear that current programmes are inadequate to reverse the epidemic among Thai men who have sex with men, unlike the 100 per cent condom campaign that led to the resounding success of the Royal Thai government in reversing the epidemic of heterosexual transmission in the mid-1990s.

8. Basic science

Adenovirus vector vaccination induces expansion of memory CD4 T cells with a mucosal homing phenotype that are readily susceptible to HIV-1.

Benlahrech A, Harris J, Meiser A, Papagatsias T, Hornig J, Hayes P, Lieber A, Athanasopoulos T, Bachy V, Csomor E, Daniels R, Fisher K, Gotch F, Seymour L, Logan K, Barbagallo R, Klavinskis L, Dickson G, Patterson S. Proc Natl Acad Sci U S A. 2009;106:19940-5. Epub 2009 Nov 16.

In the recently halted HIV type 1 (HIV-1) vaccine STEP trial, individuals that were seropositive for adenovirus serotype 5 (Ad5) showed increased rates of HIV-1 infection on vaccination with an Ad5 vaccine. The authors propose that this was due to activation and expansion of Ad5-specific mucosal-homing memory CD4 T cells. To test this hypothesis, Ad5 and Ad11 antibody titres were measured in 20 healthy volunteers. Dendritic cells (DCs) from these individuals were pulsed with replication defective Ad5 or Ad11 and co-cultured with autologous lymphocytes. Cytokine profiles, proliferative capacity, mucosal migration potential, and susceptibility to HIV infection of the adenovirus-stimulated memory CD4 T cells were measured. Stimulation of T cells from healthy Ad5-seropositive but Ad11-seronegative individuals with Ad5, or serologically distinct Ad11 vectors induced preferential expansion of adenovirus memory CD4 T cells expressing alpha(4)beta(7) integrins and CCR9, indicating a **mucosal-homing phenotype**. CD4 T-cell proliferation and IFN-gamma production in response to Ad stimulation correlated with Ad5 antibody titres. However, **Ad5 serostatus did not correlate with total cytokine production upon challenge with Ad5 or Ad11. Expanded Ad5 and Ad11 memory CD4 T cells showed an increase in CCR5 expression and higher susceptibility to infection by R5 tropic HIV-1.** This suggests that adenoviral-based vaccination against HIV-1 in individuals with pre-existing immunity against Ad5 results in **preferential expansion of HIV-susceptible activated CD4 T cells that home to mucosal tissues, increases the number of virus targets, and leads to a higher susceptibility to HIV acquisition.**

Abstract: <http://www.ncbi.nlm.nih.gov/pubmed/19918060>

Editors' note: After the STEP vaccine trial was halted in 2007 for futility when the vaccine was declared ineffective, subgroup analyses revealed that people with high levels of antibodies to the vaccine delivery system (Adenovirus serotype 5 or Ad5) were more vulnerable to acquiring HIV infection if they received the vaccine rather than the placebo. This study of their immune responses found that the vaccine vector increased the number of CD4 T cells homing to mucosa to mount defences. Once there, they were sitting ducks for HIV to infect and replicate. Whether adenovirus vectors can be used in HIV vaccine trials remains in dispute and the current HVTN 505 trial is recruiting only individuals with low Ad5 titres to avoid increasing subjects' susceptibility to HIV.

9. Implementation science

The impact of HIV scale-up on health systems: A priority research agenda.

Rabkin M, El-Sadr WM, De Cock KM; Bellagio HIV/Health Systems Working Group. J Acquir Immune Defic Syndr. 2009 Nov;52 Suppl 1:S6-11.

Collaborators: Abrams E, Cahn P, Coovadia H, De Cock KM, Dybul M, El-Sadr W, Freywhot S, Isbell M, Levine R, Melaku Z, Mermin J, Mugenyi P, Mukherjee J, Perriens J, Rabkin M, Samb B, Sewankambo N, Sinkala M, Weil D, Zewdie D.

Although much has been learned about the implementation of HIV prevention, care, and treatment services in resource-limited settings, the broader impact of the rapid scale-up of HIV programs on fragile health systems has only recently been explored. A high-level working group identified priority research questions regarding the impact of HIV scale-up on **key elements of health systems: service delivery; management; information, evidence, and strategic planning; medical products, vaccines, and technologies; health financing and payments; leadership and governance; and the behaviours of providers, consumers, and communities.** Rigorous multisectoral studies are needed if HIV program expansion to the millions still needing care and treatment is to continue, and if the synergies between vertically funded HIV programs and the health systems of which they are a part are to be maximized to strengthen nations' ability to meet all their health challenges.

Fulltext:

http://journals.lww.com/jaids/Fulltext/2009/11011/The_Impact_of_HIV_Scale_Up_on_Health_Systems__A.3.aspx

Editors' note: Citing the paucity of rigorous evidence to support a negative or positive impact of HIV scale-up on health systems and the fact that opinion has dominated the debate thus far, this paper lays out 38 priority research questions in 7 categories in what is a forward-looking research agenda. The answers to these questions will guide efforts to maximize the synergies between vertical programmes and the health systems of which they are a part in a 'diagonal approach' that attends to both disease-specific and systemic priorities.

10. HIV-2

Two Distinct Epidemics: The Rise of HIV-1 and Decline of HIV-2 Infection Between 1990 and 2007 in Rural Guinea-Bissau.

van Tienen C, van der Loeff MS, Zaman SM, Vincent T, Sarge-Njie R, Peterson I, Leligdowicz A, Jaye A, Rowland-Jones S, Aaby P, Whittle H. J Acquir Immune Defic Syndr. 2009 Oct. [Epub ahead of print]

This study set out to assess changes in HIV incidence and prevalence in Caió, a rural area of Guinea-Bissau, between 1990 and 2007. Three cross-sectional community surveys in 1990, 1997, and 2007, were conducted among adults. The prevalence of HIV-1 and of HIV-2 was estimated for each survey, and incidence rates were calculated for the first (1990-1997) and second period (1997-2007). The **HIV-1 incidence was approximately 4.5/1000 person-years in the two periods**, whereas **the HIV-2 incidence decreased from 4.7 (95% confidence interval 3.6-6.2) in**

the first to 2.0 (95% confidence interval 1.4-3.0) **per 1000 person-years in the second period** ($P < 0.001$). **HIV-1 prevalence rose from 0.5% in 1990 to 3.6% in 2007**, and **HIV-2 prevalence decreased from 8.3% in 1990 to 4.7% in 2007**. HIV-1 prevalence was less than 2% in 15 to 24 year olds in all surveys and was highest (7.2%) in 2007 among 45 to 54 year olds. The **HIV-2 prevalence was fivefold higher in older subjects** (≥ 45 yr) compared with those less than 45 years in both sexes in 2007. HIV-1 incidence is stable, and its prevalence is increasing, whereas HIV-2 incidence and prevalence are both declining. In contrast with what has been observed in other sub-Saharan countries, HIV-1 prevalence is lower in younger age groups than older age groups.

Abstract: <http://www.ncbi.nlm.nih.gov/pubmed/19841588>

Editors' note: HIV-1 has spread globally while HIV-2 remains confined to West Africa where it is thought to have originated and to countries with socio-economic links to Portugal. HIV-2 has lower sexual and vertical transmissibility, likely due to the lower levels of viraemia seen in HIV-2 infection. This study, the largest community-based study monitoring changes in incidence and prevalence of HIV-1 and HIV-2, found a decline in HIV-2 incidence over an 18 year period and lower HIV-1 incidence and prevalence in 15 to 24 year olds compared with other age groups in this rural area of Guinea-Bissau, suggesting that public health HIV prevention programming from 2002 to 2006 could have influenced risk behaviour among young people. It would be useful to conduct behavioural research and qualitative studies with young people to obtain their views on serological and behavioural findings and what they think has been most effective in protecting them from HIV infection.

Baseline characteristics, response to and outcome of antiretroviral therapy among patients with HIV-1, HIV-2 and dual infection in Burkina Faso.

Harries K, Zachariah R, Manzi M, Firmenich P, Mathela R, Drabo J, Onadja G, Arnould L, Harries A. *Trans R Soc Trop Med Hyg.* 2009. [Epub ahead of print]

In an urban district hospital in Burkina Faso Harries *et al* investigated the relative proportions of HIV-1, HIV-2 and HIV-1/2 among those tested, the baseline sociodemographic and clinical characteristics, and the response to and outcome of antiretroviral therapy (ART). A total of 7368 individuals (male=32%; median age=34 years) were included in the analysis over a 6 year period (2002-2008). The **proportions of HIV-1, HIV-2 and dual infection were 94%, 2.5% and 3.6%, respectively. HIV-1-infected individuals were younger, whereas HIV-2-infected individuals were more likely to be male, have higher CD4 counts and be asymptomatic on presentation.** Antiretroviral therapy was started in **4255 adult patients** who were **followed up for a total of 8679 person-years**, during which time **469 deaths occurred**. Mortality differences by serotype were not statistically significant, but were generally worse for HIV-2 and HIV-1/2 after controlling for age, CD4 count and WHO stage. Among severely immune-deficient patients, mortality was higher for HIV-2 than HIV-1. CD4 count recovery was poorest for HIV-2. HIV-2 and dually infected patients appeared to do less well on antiretroviral therapy than HIV-1 patients. Reasons may include differences in age at baseline, lower intrinsic immune recovery in HIV-2, use of ineffective ART regimens (inappropriate prescribing) by clinicians, and poor drug adherence.

Full text:

http://www.sciencedirect.com/science?_ob=ArticleURL&_udi=B75GP-4X962XC-3&_user=3824252&_rdoc=1&_fmt=&_orig=search&_sort=d&_docanchor=&view=c&_acct=C000055308&_version=1&_urlVersion=0&_userid=3824252&md5=e447c060389c8f3d8d3062842f79d69a

Editors' note: HIV-2 is thought of as being less pathogenic than HIV-1. People with HIV-2 have a much longer asymptomatic stage, slower progression to AIDS, a slower decline in CD4 count, and lower mortality. So why did this Burkina Faso study find poorer immunological responses to antiretroviral treatment and worse treatment outcomes in adults with HIV-2 infection? Several possibilities deserve further attention. Aside from the fact that people with HIV-1 infection tended to initiate treatment at a much earlier age, 25% of HIV-2 infected patients were given non-

nucleoside reverse transcriptase inhibitor (NNRTI) regimens when HIV-2 is naturally resistant to NNRTI. About 38% were also placed on a nelfinavir-containing regimen that has limited virological benefit in people with HIV-2. Matching viral type with treatment regimen is clearly important and it requires correct diagnosis, training, and mentoring along with adequate access to effective antiretroviral drug regimens.

11. Knowledge translation

How can we support the use of systematic reviews in policymaking?

Lavis JN. *PLoS Med.* 2009;6:e1000141. Epub 2009 Nov 17.

Policymakers need many types of research evidence—synthesized and packaged for them—and the use of this evidence supported in multiple complementary ways. Stakeholders who seek to influence the policymaking process have the same requirements. **Policymakers and stakeholders need many types of systematic reviews.** For example, reviews of qualitative studies can help to identify alternative framings of the problem, to understand how or why a policy or program option works, and to appreciate stakeholders' perspectives on particular options. Policymakers and stakeholders now have access to many review-derived products: (1) **summaries** of systematic reviews highlighting decision-relevant information; (2) **overviews** of systematic reviews providing a “map” of the policy questions addressed by systematic reviews and the insights derived from them; and (3) **policy briefs** drawing on many systematic reviews to characterize a problem, policy or program options to address the problem, and implementation strategies. A range of activities are being undertaken to support the use of reviews and review-derived products in policymaking, all of which warrant rigorous evaluation. Future challenges include: (1) examining whether and when any apparent duplication of efforts occurs in the production of review-derived products at the international level; and (2) scaling up activities that are found to be effective in supporting the use of reviews and review-derived products in policymaking.

Full text: <http://www.plosmedicine.org/article/info%3Adoi%2F10.1371%2Fjournal.pmed.1000141>

Editors' note: Informative systematic reviews of the evidence are needed at different steps in the policymaking process and can include reviews of qualitative studies of people's views to help identify alternative framings of a problem. The insights derived from reviews can compete with institutional constraints, interest group pressure, citizens' values, and policymakers' past experiences, to name some of the influences, but they should be on the table throughout the process. Political events can create windows of opportunity for the results of reviews to be considered. Factors that increase the use of research evidence in policymaking include increased interactions between researchers and policymakers, timeliness, and good agreement between research evidence and the beliefs, values, interests or political goals of policymakers. .

That was **HIV this week**, signing off.

Editors' notes on journal access

For readers in all countries:

All abstracts in *HIV This Week* are freely available on the Web.

You can access many scientific journals free of charge no matter where you are located, but for some journals you do need a subscription to access the full text of an article. Other journals offer free access to full-text articles after a certain period of time - see lists at Pubmed Central ([click here](#)) (and High Wire Press ([click here](#))).

A number of journals are free to readers in all countries through ScienceDirect ([click here](#)). Examples of open access journals are BioMed Central journals ([click here](#)) and Public Library of Science (PLoS) journals ([click here](#)).

Open Science Directory ([click here](#)) is a global search tool open access journals and journals in special programmes for developing countries.

For residents of low- and middle-income countries:

The Health InterNetwork Access to Research Initiative (HINARI), set up by the World Health Organisation (WHO) together with major publishers, enables readers at health institutions in low- and middle-income countries to gain access to one of the world's largest collections of biomedical and health literature. Over 6200 journal titles are now available to health institutions in 108 countries, benefiting many thousands of health workers and researchers, and in turn, contributing to improved world health. More information on the HINARI programme and eligible countries is available at their website ([click here](#)). Local, not-for-profit institutions in low- and middle- income countries may register for access to the journals through HINARI. Institutions in countries with GNP per capita below \$1250 are eligible for free access. Institutions in countries with GNP per capita \$1250-\$3000 pay a fee of \$1000 per year/institution.

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