

HIV This Week: what scientific journals said

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Don't forget that you can find a wealth of information on the HIV epidemic and responses to it at www.unaids.org.

1. Young people

A tale of two countries: rethinking sexual risk for HIV among young people in South Africa and the United States

Pettifor AE, Levandowski BA, Macphail C, Miller WC, Tabor J, Ford C, Stein CR, Rees H, Cohen M. *J Adolesc Health*. 2011 Sep;49(3):237-243.e1.

Pettifor and colleagues compared the sexual behaviours of young people in South Africa and the United States of America with the aim to better understand the **potential role of sexual behaviour in HIV transmission in these two countries that have strikingly different HIV epidemics**. Nationally representative, population-based surveys of young people aged 18-24 years from South Africa (n = 7548) and the USA (n = 13,451) were used for the present study. The prevalence of HIV was 10.2% in South Africa and <1% in the USA. **Young women and men in the USA reported an earlier age of first sex than those in South Africa** (mean age of coital debut for women: USA [16.5], South Africa [17.4]; for men: USA [16.4], SA [16.7]). **The median number of lifetime partners is higher in the USA than in South Africa**: women: USA (4), South Africa (2); men: USA (4), South Africa (3). **The use of condom at last sex is reported to be lower in the USA than in South Africa**: women: USA (36.1%), South Africa (45.4%); men: USA (48%), South Africa (58%). On average, **young women in South Africa report greater age differences with their sex partners** than young women in the USA. Young people in the USA report riskier sexual behaviours than young people in South Africa, despite the much higher prevalence of HIV infection in South Africa. **Factors above and beyond sexual behaviour** likely play a key role in the ongoing transmission of HIV in South African youth, and thus **should be urgently uncovered to develop maximally effective prevention strategies**.

Abstract: <http://www.ncbi.nlm.nih.gov/pubmed/21856514>

Editor's note: This comparison of two nationally representative surveys of young people starkly underscores that behaviour is not the sole determinant of HIV risk. South African young people had their first sex at a later age, have fewer sexual partners, and practise more safer sex than their American counterparts. How can the more than 10-fold difference in HIV prevalence be explained? The first thought goes to larger age gaps between sexual partners. This means sexual mixing with older partners who can act as a bridge population to younger cohorts... but there has to be more to it than that. In South Africa, male circumcision levels are far lower, herpes simplex 2 infection levels are higher, genital tract inflammation is higher, co-infections (tuberculosis, helminths) that can increase viral set points are more common, and the prevalence of the CCR5Δ32 coreceptor is lower. But social determinants, such as gender power imbalances, poverty, coerced sex and rape, lack of youth friendly services, and stigma are likely playing important roles. Although these surveys were conducted in 2003 (South Africa) and 2001-2 (USA) using somewhat different methodologies, the finding that 'ordinary' sexual behaviour can place young people, particularly young women, in South Africa at such high risk should galvanise leaders at all levels to call for urgent action. Advocates are calling out 'where the hell is the gel' and researchers are testing microfinance and conditional cash transfers, but it will take a paradigm shift at all levels to prioritise investment in protecting young people from what is a preventable, chronic, lifelong disease.

2. Hormonal contraception

Use of hormonal contraceptives and risk of HIV-1 transmission: a prospective cohort study

Renee Heffron, Deborah Donnell, Prof Helen Rees, Connie Celum, Nelly Mugo, Edwin Were, Guy de Bruyn, Edith Nakku-Joloba, Kenneth Ngunjiri, James Kiarie, Robert W Coombs, Jared M Baeten, *The Lancet Infectious Diseases*, Early Online Publication, 4 October 2011

Hormonal contraceptives are used widely but their effects on HIV-1 risk are unclear. Heffron and colleagues aimed to assess the association between **hormonal contraceptive use and risk of HIV-1 acquisition** by women and **HIV-1 transmission** from HIV-1-infected women to their male partners. In this prospective study, they followed up **3790 heterosexual HIV-1-serodiscordant couples** participating in **two longitudinal studies of HIV-1 incidence in seven African countries**. Among injectable and oral hormonal contraceptive users and non-users, they compared rates of HIV-1

acquisition by women and HIV-1 transmission from women to men. The primary outcome measure was HIV-1 seroconversion. Cox proportional hazards regression and marginal structural modelling were used to assess the effect of contraceptive use on HIV-1 risk. **Among 1314 couples in which the HIV-1-seronegative partner was female** (median follow-up 18.0 [IQR 12.6–24.2] months), **rates of HIV-1 acquisition were 6.61 per 100 person-years in women who used hormonal contraception and 3.78 per 100 person-years in those who did not** (adjusted hazard ratio 1.98, 95% CI 1.06–3.68, p=0.03). **Among 2476 couples in which the HIV-1-seronegative partner was male** (median follow-up 18.7 [IQR 12.8–24.2] months), **rates of HIV-1 transmission from women to men were 2.61 per 100 person-years in couples in which women used hormonal contraception and 1.51 per 100 person-years in couples in which women did not use hormonal contraception** (adjusted hazard ratio 1.97, 95% CI 1.12–3.45, p=0.02). Marginal structural model analyses generated much the same results to the Cox proportional hazards regression. **Women should be counselled about potentially increased risk of HIV-1 acquisition and transmission with hormonal contraception**, especially injectable methods, and about the **importance of dual protection with condoms to decrease HIV-1 risk**. Non-hormonal or low-dose hormonal contraceptive methods should be considered for women with or at-risk for HIV-1.

Abstract: <http://www.sciencedirect.com/science/article/pii/S147330991170247X>

Editor's note: The issue of hormonal contraception and HIV risk continues to perplex. Observational studies have both suggested a link and not found one. This study of HIV serodiscordant couples was not specifically designed to examine this issue and had too few women on contraceptive pills to draw any conclusions. However, a doubling of the risk of HIV acquisition for HIV-negative women using injectable DMPA (depot-medroxyprogesterone acetate) and a doubling of the risk of HIV transmission from HIV-positive women using DMPA to their seronegative partners are cause for concern. Contraception improves the health of women and children worldwide and it plays a crucial role in helping women with, or at risk of, HIV infection to prevent the adverse social and health consequences of unintended pregnancies. WHO and partners are convening a technical consultation in early 2012 to re-examine the totality of evidence on the potential effects of hormonal contraception and of intrauterine devices on HIV acquisition, disease progression, and infectivity/transmission to sexual partners. The need to conduct randomized controlled trials to determine whether hormonal contraception increases the risk of HIV acquisition in women and/or of HIV transmission to men will be assessed, along with feasibility. In the meantime, we need to reinforce the importance of correct and consistent condom use, regardless of whether another method of contraception is being used. It is and has been for decades the 'dual protection' message.

3. Sexual transmission

Risk for HIV and unprotected sexual behaviour in male primary partners of transgender women

Operario D, Nemoto T, Iwamoto M, Moore T. Arch Sex Behav. 2011 May 21.

Men who have sex with transgender women are a potentially high-risk population for HIV and other sexually transmitted infections. Operario and colleagues administered structured quantitative surveys to 174 men whose primary partner was a transgender woman. They assessed men's demographic characteristics, sexual behaviours, substance use, and social-psychological factors, including condom use self-efficacy and depression. **Overall, 19% reported being HIV-positive** (8% had been diagnosed with AIDS), 11% had at least one other sexually transmitted infection during the past year, and **16% reported being in a HIV serodiscordant relationship with their primary partner**. In the **past 3 months, 40% had unprotected anal or vaginal sex with any partner**. In multivariate analysis, significant correlates of having unprotected sex included younger age, concurrent partnerships, alcohol intoxication, and low condom use self-efficacy; depression was marginally associated with having unprotected sex. Interventions are needed to reduce risk for HIV and other sexually transmitted infections among men who have sex with transgender women. Prevention programmes for these men should **build condom use self-efficacy and address the contributions of alcohol intoxication, concurrent sex partnerships, and depression to sexual risk behaviour**.

Abstract: <http://www.ncbi.nlm.nih.gov/pubmed/21604064>

Editor's note: A study of men in primary relationships with transgender women is very rare. Being in a 'primary relationship' was defined as two adults committed to each other above anyone else. The couples were identified through snowball referral techniques (Do you know couples like yours that could be interested in the study? Could you refer them to us?) and through direct approaches to couples in bars, nightclubs, book stores, community based organisations, health clinics, parks, and street locations where study advertisements were posted. The average relationship duration was 2.9 years and 47% of the couples in this convenience sample lived together. This paper describes the male partners—they reported being bisexual (45%), homosexual (23%), heterosexual (23%), and other or not willing to categorise themselves (9%). Men whose primary partner was post-operative were more likely than those with a pre-operative transgender partner to identify as heterosexual (53% vs. 20%). Overall 58% of the men in this San Francisco Bay area study described the relationship as monogamous, however one in five of them, and 12% of their transgender partners, had sex with an outside partner during the current primary partnership. Whether or not these couples are serodiscordant (one in six are), couples-based interventions aimed at strengthening safer sex practices are warranted, without preconceived assumptions about the sexual orientation of the men.

4. Male circumcision

Adult male circumcision as an intervention against HIV: an operational study of uptake in a South African community (ANRS 12126)

Lissouba P, Taljaard D, Rech D, Dermaux-Msimang V, Legeai C, Lewis D, Singh B, Puren A, Auvert B. BMC Infect Dis. 2011 Sep 26;11(1):253.

The objective of this study was to evaluate the knowledge, attitudes, and beliefs about adult male circumcision, assess the association of adult male circumcision with HIV incidence and prevalence, and **estimate adult male circumcision uptake** in a Southern African community. A cross-sectional biomedical survey (ANRS-12126) was conducted in 2007-2008 among a **random sample of 1198 men aged 15 to 49 from Orange Farm (South Africa)**. Face-to-face interviews were conducted by structured questionnaire. Recent HIV infections were evaluated using the BED incidence assay. **Circumcision status was self-reported and clinically assessed.** Adjusted HIV incidence rate ratios and prevalence ratios were calculated using Poisson regression. The response rate was 73.9%. Most respondents agreed that circumcised men could become HIV infected and needed to use condoms, although 19.3% (95%CI: 17.1% to 21.6%) asserted that adult male circumcision protected fully against HIV. **Among self-reported circumcised men, 44.9% (95%CI: 39.6% to 50.3%) had intact foreskins. Men without foreskins had lower HIV incidence and prevalence than men with foreskins** (aIRR=0.35; 95%CI: 0.14 to 0.88; aPR=0.45, 95%CI: 0.26 to 0.79). No significant difference was found between self-reported circumcised men with foreskins and other uncircumcised men. Intention to undergo adult male circumcision was associated with ethnic group and partner and family support of adult male circumcision. **Uptake of adult male circumcision was 58.8%** (95%CI: 55.4% to 62.0%). Adult male circumcision uptake in this community is high but communication and counselling should emphasize what clinical adult male circumcision is and its effect on HIV acquisition. These findings suggest that adult male circumcision roll-out is promising but requires **careful implementation strategies** to be successful against the African HIV epidemic.

Abstract: <http://www.ncbi.nlm.nih.gov/pubmed/21943076>

Editor's note: This first study to examine uptake of voluntary medical male circumcision (VMMC) among a random sample of the general population produced interesting findings. The most salient are the 55% lower HIV prevalence and 65% lower incidence in clinically circumcised men – the latter is more than the risk reduction of 60% seen in the randomised controlled trial conducted before 2005 in the same setting. More important from the point of view of programming is that 45% of men who reported that they were circumcised were found to have foreskins when they were examined. Men who have undergone initiation rituals may call themselves circumcised even if they have an intact foreskin. This suggests the importance of community education for both men and women, perhaps involving photos, about what a circumcised penis looks, along with information on the benefits of VMMC in high HIV prevalence settings. 81% of uncircumcised men in the study stated their intention to undergo VMMC and 72% of

these were circumcised through the study (59% uptake). The most important factors influencing the decision to undergo VMMC were being from a traditionally circumcising ethnic group, believing that VMMC was safe, and having partner and family support.

Acceptability of medical male circumcision in the traditionally circumcising communities in Northern Tanzania

Wambura M, Mwanga JR, Masha JF, Mshana G, Masha F, Changalucha J. BMC Public Health. 2011 May 23;11:373

Data from traditionally circumcising communities show that non-circumcised males and those circumcised in the medical settings are stigmatised. This is because **traditional circumcision embodies local notions of bravery as anaesthetics are not used**. This study was conducted to assess the acceptability of safe medical circumcision before the onset of sexual activity for HIV infection risk reduction in a traditionally circumcising community in Tanzania. A cross-sectional study was conducted among males and females aged 18-44 years in traditionally circumcising communities of Tarime District in Mara Region, North-eastern Tanzania. A face-to-face questionnaire was administered to females to collect information on the **attitudes of women towards circumcision and the preferred age for circumcision**. A similar questionnaire was administered to males to collect information on socio-demographic, preferred age for circumcision, factors influencing circumcision, client satisfaction, complications and beliefs surrounding the practice. Results were available for 170 males and 189 females. **Of the males, 168 (98.8%) were circumcised and 61 (36.3%) of those circumcised had the procedure done in the medical setting**. Of those interviewed, **165 (97.1%) males and 179 (94.7%) females supported medical male circumcision for their sons**. Of these, **107 (64.8%) males and 130 (72.6%) females preferred prepubertal medical male circumcision (12 years or less)**. Preference for prepubertal circumcision was significantly associated with non-Kurya ethnic group, circumcision in the medical setting and residence in urban areas for males in the adjusted analysis. For females, preference for prepubertal circumcision was significantly associated with non-Kurya ethnic group and being born in urban areas in the adjusted analysis. There is **a shift of preference from traditional male circumcision to medical male circumcision in this traditionally circumcising population**. However, this preference has not changed the circumcision practices in the communities because of the community social pressure. The male circumcision national programme should **take advantage of this preference for medical male circumcision by introducing safe and affordable circumcision services** and mobilising communities in a culturally sensitive manner to take up circumcision services.

Abstract: <http://www.ncbi.nlm.nih.gov/pubmed/21605433>

Editor's note: Given the numbers of male circumcisions that the 13 priority countries in sub-Saharan Africa are aiming to complete by 2015, many people believe that less attention should be given to communities that have high male circumcision prevalence already through traditional circumcising practices. This study suggests that these communities should not be left behind. Parents are concerned about bleeding, delays in wound healing, and adverse events. They also would prefer that the procedure be done before sexual activity starts. Although 97% of men and 95% of women in this study supported voluntary medical male circumcision (VMMC) for their sons, 64% of men had been circumcised traditionally and uptake of VMMC is low due to social pressure and increased cost. If safe, affordable, and culturally sensitive VMMC services were made available, as they have been elsewhere in parts of Africa that practice traditional circumcision, it would not be long before parents and young people align their actions with their preferences. There will be more on male circumcision in the next issue of HIV This Week, but in the meantime, do check out the Joint Strategic Action Framework on Voluntary Medical Male Circumcision that was launched by UNAIDS and PEPFAR on behalf of WHO and other partners last week at the International Conference on AIDS and Sexually Transmitted Infections in Africa held in Addis Ababa, Ethiopia. You can find it at: http://www.unaids.org/en/media/unaids/contentassets/documents/unaidspublication/2011/JC2251_Action_Framework_circumcision_en.pdf

5. HIV and older people

HIV attitudes, awareness and testing among older adults in Africa

Negin J, Nemser B, Cumming R, Lelera E, Ben Amor Y, Pronyk P. AIDS Behav. 2011 Jul 8.

In Africa, older **adults aged 50 and older** are still sexually active and play a critical role as caregivers, yet little is known about their attitudes towards HIV and awareness of services. In this study, **surveys were conducted in nine African sites**. A multilevel model was fitted to evaluate the relationship between age and outcome variables. The study reveals that **people aged 50 years and older have lower levels of HIV-related knowledge and awareness than those aged 25-49**. Older adults were **less likely to have been tested for HIV** and women aged 50 and older showed particularly low levels of awareness.

Abstract: <http://www.ncbi.nlm.nih.gov/pubmed/21739287>

Editor's note: In 2010, a study estimated that 3 million people aged 50 and over were living with HIV in sub-Saharan Africa, representing fully 14% of those over age 15 with HIV infection. Some of these people have aged into this age category due to the life-prolonging benefits of antiretroviral therapy but others are becoming newly infected each day. Many do not know that they have HIV infection. Why do we never hear about older people with HIV? Our HIV prevention progress indicators for sexual transmission refer to people aged 15-49 years and prevalence data collected through Demographic and Health Surveys (DHS) and presented by UNAIDS do not include people aged 50 years and older. This measurement neglect is reflected in lack of programming to raise awareness and knowledge levels, develop communication and condom negotiation skills, and address stigma and discrimination in this age group commonly seen primarily as a caregiver source. Some countries are jumping ahead: South Africa has held caregiver workshops to improve attitudes and knowledge and has added males older than 50 to its list of most-at-risk populations (key populations). Across the nine clusters in eight countries in this Millennium Villages Project study, the lowest 'ever tested for HIV' levels were in Senegal (0% for both men and women) and the highest in Rwanda (23% for men and 17% for women). More attention to people aged 50 and older is needed now if they are to avoid HIV infection, access HIV testing, start timely antiretroviral treatment, and have a positive intergenerational influence on community attitudes and knowledge as sexually active and informed educators, as well as caretakers.

6. Financing

Has HIV/AIDS displaced other health funding priorities? Evidence from a new dataset of development aid for health

Lordan G, Tang KK, Carmignani F. Soc Sci Med. 2011 Jul 9.

In recent times there has been a **sense that HIV control has been attracting a significantly larger portion of donor health funding** to the extent that it crowds out funding for other health concerns. Although there is no doubt that **HIV has absorbed a large share of development assistance for health**, whether HIV is actually diverting funding away from other health concerns has yet to be analyzed fully. To fill this vacuum, this study aims to test if a higher level of HIV funding is related to a displacement in funding for other health concerns, and if yes, to quantify the magnitude of the displacement effect. Specifically, Lordan and colleagues **consider whether HIV development assistance for health has displaced i) TB, ii) malaria iii) health sector and 'other' development assistance** for health in terms of the dollar amount received for aid. They consider this question within a regression framework controlling for time and recipient heterogeneity. **The authors find displacement effects for malaria and health sector funding but not TB. In particular, the displacement effect for malaria is large and worrying.**

Abstract: <http://www.ncbi.nlm.nih.gov/pubmed/21745705>

Editor's note: This study of 44 low- and middle-income countries that have a significant burden of HIV, tuberculosis (TB), and malaria, along with a health sector in need of strengthening, assessed the extent of dollar displacement, rather than share displacement, that donor HIV funding may be incurring. This

means that it examined changes in the actual amount of aid provided for HIV, TB, malaria, and health sector strengthening, rather than changes in the share of aid devoted specifically to HIV. As we know, the amount of development assistance for health (DAH) devoted to HIV has increased over time. TB has not suffered, perhaps because donors see funding for the two diseases to be complementary. Malaria, killing one million people in 2008 and accounting for 20% of African childhood mortality, clearly ranks highly for donor attention by the criteria of burden of disease. As well, lower per-capita income in high malaria-burden countries suggests less capacity for domestic resource mobilisation for malaria. Yet, this study estimates that for every 1% increase in funds devoted to HIV in a year, there is an 11% decrease the following year in funds devoted to malaria. This rises to 19% when considering only the 29 countries with malaria prevalence above 1% of the population. Aside from the concern about likely 'crowding out' of malaria funding by HIV funding, this study suggests that donor commitments are barely medium-term, let alone long-term, a factor that is undermining country-led processes for resource allocation planning for both diseases.

Long-term costs and health impact of continued global fund support for antiretroviral therapy

Stover J, Korenromp EL, Blakley M, Komatsu R, Viisainen K, Bollinger L, Atun R. *PLoS One*. 2011;6(6):e21048.

By the end of 2011 Global Fund investments will be supporting 3.5 million people on antiretroviral therapy in 104 low- and middle-income countries. Stover and colleagues estimated the **cost and health impact of continuing treatment for these patients through 2020**. Survival on first-line and second-line antiretroviral therapy regimens is estimated based on annual retention rates reported by national AIDS programmes. **Costs per patient-year were calculated from country-reported antiretroviral procurement prices, and expenditures on laboratory tests, health care utilisation, and end-of-life care from in-depth costing studies**. Of the 3.5 million patients on antiretroviral therapy in 2011, 2.3 million will still need treatment in 2020. **The annual cost of maintaining antiretroviral therapy falls from \$1.9 billion in 2011 to \$1.7 billion in 2020**, as a result of a **declining number of surviving patients partially offset by increasing costs as more patients migrate to second-line therapy**. The Global Fund is expected to continue being a major contributor to meeting this financial need, alongside other international funders and domestic resources. **Costs would be \$150 million less in 2020 with an annual 5% decline in first-line ARV prices and \$150-370 million less with a 5%-12% annual decline in second-line prices**, but **\$200 million higher in 2020 with phase out of stavudine (d4T)**, or **\$200 million higher with increased migration to second-line regimens expected if all countries routinely adopted viral load monitoring**. Deaths postponed by antiretroviral therapy correspond to **830,000 life-years saved in 2011, increasing to around 2.3 million life-years every year between 2015 and 2020**. Annual patient-level direct costs of supporting a patient cohort remain fairly stable over 2011-2020, if current antiretroviral prices and delivery costs are maintained. **Second-line antiretroviral prices are a major cost driver, underscoring the importance of investing in treatment quality to improve retention on first-line regimens**.

Abstract: <http://www.ncbi.nlm.nih.gov/pubmed/21731646>

Editor's note: This analysis of the cost and impact of continuing treatment for the 3.5 million of people who are co-supported by the Global Fund, compared to stopping it, provides food for thought. For the 6.6 million people on antiretroviral therapy now, retention on treatment is excellent after the first year, based on data from 38 national AIDS programmes in 2008: 80% not dying or lost to follow-up at 1 year, 75% at 2 years, 74% at 3 years, and 73% at 4 years. If treatment were to be stopped now for those receiving it, 18% would die in the first year, 46% after two years, 64% after three years, 76% after 4 years, 84% after 5 years, and 97% after 6 years. Median survival after treatment cessation would be 2 to 3 years. If the Global Fund did not support any new people to start antiretroviral therapy, the costs to maintain those already on treatment through to 2020 would decline. Costs increase as more people are moved off d4T first-line regimens or start costly second-line regimens (24% will likely be on second-line by 2020), however deaths result in 10% reduced costs overall. Antiretroviral drugs constitute 42% of first-line regimen and 81% of second-line regimen costs, underscoring the importance of further price reductions. Routine viral load testing, CD4 counts, and clinical monitoring for timely detection of and responses to adherence difficulties, will prevent unnecessary switching to second-line regimens. The

most striking finding is the number of life-years saved each year—it rises to 2.3 million by 2017 when virtually everyone treated today would have died in the absence of treatment. Setting aside moral, ethical, and treatment for prevention arguments, continued and increased investment in antiretroviral treatment makes economic sense, not only for those already on treatment but also for those eligible and waiting.

7. Drug resistance

HIV-1 drug resistance in antiretroviral-naive individuals in sub-Saharan Africa after rollout of antiretroviral therapy: a multicentre observational study

Hamers RL, Wallis CL, Kityo C, Siwale M, Mandaliya K, Conradie F, Botes ME, Wellington M, Osibogun A, Sigaloff KC, Nankya I, Schuurman R, Wit FW, Stevens WS, van Vugt M, de Wit TF; for PharmAccess African Studies to Evaluate Resistance (PASER). *Lancet Infect Dis*. 2011 Oct;11(10):750-9.

There are few data on the epidemiology of primary HIV-1 drug resistance after the roll-out of antiretroviral treatment in sub-Saharan Africa. Hamers and colleagues aimed to assess the **prevalence of primary resistance in six African countries after antiretroviral treatment roll-out** and if wider use of antiretroviral treatment in sub-Saharan Africa is associated with rising prevalence of drug resistance. They did a cross-sectional study in antiretroviral-naive adults infected with HIV-1 who had not started first-line antiretroviral treatment, recruited between 2007 and 2009 from 11 regions in Kenya, Nigeria, South Africa, Uganda, Zambia, and Zimbabwe. They did **population-based sequencing of the pol gene on plasma specimens** with greater than 1000 copies per mL of HIV RNA. They identified drug-resistance mutations with the WHO list for transmitted resistance. The prevalence of sequences containing at least one drug-resistance mutation was calculated accounting for the sampling weights of the sites. They assessed the risk factors of resistance with multilevel logistic regression with random coefficients. 2436 (94.1%) of 2590 participants had a pretreatment genotypic resistance result. 1486 participants (57.4%) were women, 1575 (60.8%) had WHO clinical stage 3 or 4 disease, and the median CD4 count was 133 cells per μ L (IQR 62-204). **Overall sample-weighted drug-resistance prevalence was 5.6%** (139 of 2436; 95% CI 4.6-6.7), **ranging from 1.1%** (two of 176; 0.0-2.7) **in Pretoria, South Africa, to 12.3%** (22 of 179; 7.5-17.1) **in Kampala, Uganda**. The pooled prevalence for all three Ugandan sites was 11.6% (66 of 570; 8.9-14.2), compared with 3.5% (73 of 1866; 2.5-4.5) for all other sites. **Drug class-specific resistance prevalence was 2.5%** (54 of 2436; 1.8-3.2) **for nucleoside reverse-transcriptase inhibitors (NRTIs), 3.3%** (83 of 2436; 2.5-4.2) **for non-NRTIs (NNRTIs), 1.3%** (31 of 2436; 0.8-1.8) **for protease inhibitors, and 1.2%** (25 of 2436; 0.7-1.7) **for dual-class resistance to reverse-transcriptase inhibitors and non-reverse transcriptase inhibitors**. The most common drug-resistance mutations were **K103N** (43 [1.8%] of 2436), **thymidine analogue mutations** (33 [1.6%] of 2436), **M184V** (25 [1.2%] of 2436), and **Y181C/I** (19 [0.7%] of 2436). **The odds ratio for drug resistance associated with each additional year since the start of the antiretroviral treatment roll-out in a region was 1.38** (95% CI 1.13-1.68; $p=0.001$). The higher prevalence of primary drug resistance in Uganda than in other African countries is probably related to the earlier start of antiretroviral treatment roll-out in Uganda. Resistance surveillance and prevention should be prioritised in settings where antiretroviral treatment programmes are scaled up.

Abstract: <http://www.ncbi.nlm.nih.gov/pubmed/21802367>

Editor's note: PASER-M is a multicentre prospective cohort of people receiving first- or second-line antiretroviral therapy in 13 clinical sites in 6 African countries. Pre-treatment viral loads in 2436 people who were antiretroviral-naïve were sequenced for drug resistance giving a weighted prevalence result of 5.6%. The lowest prevalence was in Pretoria (1.1%) and the highest was in Kampala (12.3%). South Africa is the only country with routine viral load monitoring while Uganda is the country with the oldest history of antiretroviral treatment. These findings emphasise the importance of viral load monitoring. Without it, many people are unnecessarily switched to more expensive and toxic second-line therapies or remain on failing first-line regimens that can provoke drug resistance. Onward transmission of drug-resistant strains can compromise the effectiveness of the first-line regimens that are part of the public health approach (2 NRTIs and one NNRTI). Pre-treatment drug resistance testing is used in high-income countries where 9 to 15% of antiretroviral-naïve people have at least one drug-resistant variant in order

to guide individual treatment choices. At a minimum, low- and middle-income countries need to move rapidly to routine viral load monitoring to reduce the risk of resistance undermining treatment programme successes.

8. Social determinants

Addressing social drivers of HIV/AIDS for the long-term response: conceptual and methodological considerations

Auerbach JD, Parkhurst JO, Cáceres CF. Glob Public Health. 2011 Jul 11.

A key component of the **shift from an emergency to a long-term response** to AIDS is a change in focus from HIV prevention interventions focused on individuals to a comprehensive strategy in which **social/structural approaches are core elements**. Such approaches aim to modify social conditions by **addressing key drivers of HIV vulnerability** that affect the ability of individuals to protect themselves and others from HIV. The development and implementation of evidence-based social/structural interventions have been hampered by both scientific and political obstacles that have not been fully explored or redressed. This paper provides a framework, examples, and some guidance for **how to conceptualise, operationalise, measure, and evaluate complex social/structural approaches to HIV prevention** to help situate them more concretely in a long-term strategy to end AIDS.

Abstract: <http://www.ncbi.nlm.nih.gov/pubmed/21745027>

Editor's note: The critical role of social determinants of health in shaping people's decisions to act, i.e. their agency, has been recognised for a long time. These determinants include social and structural factors, such as poverty, gender inequality, and human rights violations that increase people's vulnerability to HIV. But what are the social and structural factors that contribute to the resilience of individuals, communities, and societies against HIV? The first step in better understanding vulnerability and resilience is to assess context-specific contributing/influencing factors. These can then inform the development of a socially plausible hypothesis of causal chains linked to HIV transmission, with intervention possibilities to consider at various levels, from the most proximal to the most distal. Distal level structural interventions may institute policy-legal changes, create or reinforce environmental enablers, produce changes in harmful social norms, catalyse social and political change, and introduce economic initiatives. The challenges of evaluating the impact of structural interventions on HIV incidence are daunting but both quantitative and qualitative social science methods can start by assessing impact more generally. It is important to recall that virtually all of these social changes are important from a social justice viewpoint. UNAIDS succinct definition of combination prevention underscores the importance of integrating strategies to address social determinants: '...the strategic, simultaneous use of different classes of prevention activities (biomedical, behavioural, social/structural) that operate on multiple levels (individual, relationship, community, societal) to respond to the specific needs of particular audiences...through prioritising, partnerships, and engagement of affected communities.'

9. Basic science

Crystal structure of a monomeric retroviral protease solved by protein folding game players

Khatib F, Dimaio F, Cooper S, Kazmierczyk M, Gilski M, Krzywda S, Zabranska H, Pichova I, Thompson J, Popović Z, Jaskolski M, Baker D. Nat Struct Mol Biol. 2011 Sep 18. [Epub ahead of print]

Following the **failure of a wide range of attempts to solve the crystal structure of M-PMV retroviral protease** by molecular replacement, Khatib and colleagues **challenged players of the protein folding game Foldit** to produce accurate models of the protein. Remarkably, **Foldit players were able to generate** models of sufficient quality for **successful molecular replacement and subsequent structure determination**. The refined structure provides **new insights for the design of antiretroviral drugs**.

Abstract: <http://www.ncbi.nlm.nih.gov/pubmed/21926992>

Editor's note: Who would have thought that gamers would bring their human intuition and three-dimensional pattern-making skills to the table and solve a persistent molecular science challenge, ending up as co-authors on a scientific paper in the prestigious journal *Nature Structural and Molecular Biology*! With names like spvincent, grabhorn, and mimi, Foldit players from two teams, the Foldit Contenders and the Foldit Void Crushers, competed over a 3-week period to solve the crystal structure of a retroviral protease. This is an important objective: significant pharmaceutical attention is focused on developing antiretroviral drugs against these enzymes—they are key to the maturation and multiplication of HIV. However, despite concerted efforts, this work has been hampered by complete failure over the past decade to determine the crystal structures of retroviral proteases. This first striking success opens the door to more integration of game-player ingenuity into scientific inquiry. This specific approach to on-line crowdsourcing could see on-line game players solving many more scientific problems – what a potentially great marriage of skills and challenges!

Zinc-finger nucleases for somatic gene therapy: the next frontier

Rahman SH, Maeder ML, Joung JK, Cathomen T. Hum Gene Ther. 2011 Aug;22(8):925-33.

Zinc-finger nucleases are a powerful tool that can be used to edit the human genome *ad libitum*. The technology has experienced remarkable development in the last few years with regard to both the target site specificity and the engineering platforms used to generate zinc-finger proteins. As a result, **two phase I clinical trials aimed at knocking out the CCR5 receptor in T cells isolated from HIV patients to protect these lymphocytes from infection with the virus have been initiated.** Moreover, zinc-finger nucleases have been successfully employed to knockout or correct disease-related genes in human stem cells, including hematopoietic precursor cells and induced pluripotent stem cells. **Targeted genome engineering approaches** in multipotent and pluripotent stem cells hold great promise for future strategies geared toward correcting inborn mutations for personalized cell replacement therapies. This review describes how zinc-finger nucleases have been applied to models of gene therapy, discusses the opportunities and the risks associated with this novel technology, and suggests future directions for their safe application in therapeutic genome engineering.

Abstract: <http://www.ncbi.nlm.nih.gov/pubmed/21631241>

Editor's note: What are zinc-finger nucleases and why should we care? Zinc finger nucleases are artificial nucleases that have two functional domains—one to recognize DNA and the other to cut it. They can cleave DNA, breaking both strands, at a specifically chosen target gene. Double-stranded breaks trigger one of two damage responses—one simply puts the DNA back together while the other uses a donor DNA sequence to repair the break and correct a pre-existing genetic defect at the same time. This is not science fiction. Several knockout animal models have been created, such as the SCID (severe combined immunodeficiency) rat, that permit the study of various diseases. Two phase 1 trials are underway in people living with HIV to assess the safety of zinc-finger-nuclease knockout of the CCR5 receptor on chromosome 3. When this CD4+ cell receptor is deformed or absent, as in the naturally occurring CCR5deltaΔ mutation, people are largely protected from HIV infection. The idea is to reduce the capacity of HIV to dock and enter target cells. There is still much to learn, for example, to prevent the vectors carrying zinc-finger nucleases from integrating into our own genome and to ensure efficient and precise targeting of the correct DNA sites. Zinc-finger nucleases represent a promising advance—a tool to edit the human genome—that should get us all thinking about what the future might look like!

10. Orphans and vulnerable children

Parental loss, trusting relationship with current caregivers, and psychosocial adjustment among children affected by AIDS in China

Zhao J, Li X, Barnett D, Lin X, Fang X, Zhao G, Naar-King S, Stanton B. Psychol Health Med. 2011 Aug;16(4):437-49.

The objective of this study was to examine the relationship between parental loss, trusting relationship with current caregivers, and psychosocial adjustment among children affected by AIDS in China. In this

study, cross-sectional data were collected from **755 AIDS orphans (296 double orphans and 459 single orphans), 466 vulnerable children living with HIV-infected parents, and 404 comparison children in China**. The trusting relationship with current caregivers was measured with a 15-item scale (Cronbach's $\alpha = 0.84$) modified from the Trusting Relationship Questionnaire developed by Mustillo et al. in 2005 (Quality of relationships between youth and community service providers: Reliability and validity of the trusting relationship questionnaire. *Journal of Child and Family Studies*, 14, 577-590). The **psychosocial measures** include **rule compliance/acting out, anxiety/withdrawal, peer social skills, school interest, depressive symptoms, loneliness, self-esteem, future expectation, hopefulness about future, and perceived control over the future**. Group mean comparisons using analysis of variance suggested a significant association ($p < 0.0001$) between the trusting relationship with current caregivers and all the psychosocial measures, except anxiety and depression. These associations remained significant in General Linear Model analysis, controlling for children's gender, age, family socioeconomic status, orphan status (orphans, vulnerable children, and comparison children), and appropriate interaction terms among factor variables. The findings in the current study support the global literature on the **importance of attachment relationship with caregivers in promoting children's psychosocial development**. Future prevention intervention efforts to improve AIDS orphans' psychosocial well-being will need to take into consideration the **quality of the child's attachment relationships with current caregivers and help their current caregivers to improve the quality of care for these children**. Future study is needed to explore the possible reasons for the lack of association between a trusting relationship and some internalizing symptoms such as anxiety and depression among children affected by HIV.

Abstract:<http://www.ncbi.nlm.nih.gov/pubmed/21749241>

Editor's note: This study was conducted among children in two of the villages most affected by the HIV epidemic that was caused by unhygienic blood donation practices in the late 80s to mid 90s in Central China. Rural farmers donated blood without being tested for HIV, hepatitis B and C, or other blood borne infections under conditions of reuse of needles and contaminated equipment. Blood from several plasma donors of the same blood type was pooled and the plasma separated out before the donors were re-injected with the saved, potentially contaminated blood cells to prevent anaemia. The orphaned children in this study were double orphans living in four government-funded orphanages (23%), eight group home settings with community volunteer 'house parents' taking care of them (4%), or in family/kinship care (12%). The single orphans (61%) were in family/kinship care. Two points are key. First, the culturally adapted version of the Trusting Relationship Questionnaire used in this study for the first time in China is a valid assessment tool for children of various ages and different sexes, who are living in a variety of situations. Second, there was a strong relationship between trusting relationship and psychosocial adjustment, independent of family HIV experiences, sex, age, and family socio-economic status. This resonates for everyone, everywhere—a positive attachment relationship in childhood is key to developing trust, having confidence in oneself, and being resilient in the face of adversity and loss, including losing a parent or both parents to HIV.

11. Treatment

Epidemiological characteristics and predictors of late presentation of HIV infection in Barcelona (Spain) during the period 2001-2009

Garcia de Olalla P, Mazardo C, Sambeat MA, Ocana I, Knobel H, Humet V, Domingo P, Ribera E, Guelar A, Marco A, Belza MJ, Miro JM, Cayla1 JA, Hivsg TH. AIDS Res Ther. 2011 Jul 6;8(1):22.

Early diagnosis of HIV infection can prevent morbidity and mortality as well as reduce HIV transmission. The aim of the present study was to assess prevalence, describe trends and identify factors associated with **late presentation of HIV infection in Barcelona (Spain) during the period 2001-09**. Demographic and epidemiological characteristics of cases reported to the Barcelona HIV surveillance system were analysed. **Late presentation** was defined for individuals with a **CD4 count below 350 cells/ml upon HIV diagnosis or diagnosis of AIDS within 3 months of HIV diagnosis**. Multivariate logistic regression was used to identify predictors of late presentation. Of the 2,938 newly diagnosed HIV-infected individuals, 2507 (85,3%) had either a CD4 cell count or an AIDS diagnosis available. **A total of 1139 (55.6%) of the 2507 studied cases over these nine years were late presenters** varying

from **48% among men who have sex with men to 70% among heterosexual men**. The proportion of late presentation was 62.7% in 2001-2003, 51.9% in 2004-2005, 52.6% in 2006-2007 and 52.1% in 2008-2009. A decrease over time only was observed between 2001-2003 and 2004-2005 ($p=0.001$) but remained constant thereafter ($p=0.9$). **Independent risk factors for late presentation were older age at diagnosis** ($p<0.0001$), **use of injected drugs by men** ($p<0.0001$), **being a heterosexual man** ($p<0.0001$), and **being born in South America** ($p<0.0001$) or **sub-Saharan Africa** ($p=0.002$). Late presentation of HIV is still too frequent in all transmission groups in spite of a strong commitment with HIV prevention in Barcelona. It is necessary to develop interventions that increase HIV testing and facilitate earlier entry into HIV care.

Abstract: <http://www.ncbi.nlm.nih.gov/pubmed/21729332>

Editor's note: Since 1987, Barcelona has had an active AIDS surveillance system collecting information from physicians about new AIDS diagnoses, hospitals about AIDS discharge diagnoses, tuberculosis registers about patients with AIDS, and vital statistics bureaux about AIDS deaths. In 2001, an HIV surveillance system was added to collect information about new HIV diagnoses, using a unique patient identifier to minimise double counting. The 9-year trends of newly diagnosed HIV infections show increasing proportions of men who have sex with men (40% in 2001-3 to 62% in 2008-9) and increasing proportions of migrants (23% to 46%) having arrived in Spain from less than a year to more than 10 years previously. Men who have sex with men were less likely to present late than men who inject drugs (48% versus 66%), with the latter having the longest delays between HIV diagnosis and the first CD4 count that could trigger initiation of antiretroviral therapy (162 days versus 54 days for others), possibly because the drug rehabilitation centres and prisons where they learned their HIV status did not have accessible CD4 count testing. Overall, for each increase in age of 5 years, the risk of presenting late increased 38%—older people and their physicians are clearly not thinking about HIV. Surveillance systems such as these in Barcelona can inform the tailoring of programmes aimed at earlier entry into HIV care and treatment to decrease HIV progression, stimulate immune recovery, and reduce onward transmission.

12. Maternal and child mortality

Progress towards Millennium Development Goals 4 and 5 on maternal and child mortality: an updated systematic analysis

Lozano R, Wang H, Foreman KJ, Rajaratnam JK, Naghavi M, Marcus JR, Dwyer-Lindgren L, Lofgren KT, Phillips D, Atkinson C, Lopez AD, Murray CJ. *Lancet*. 2011 Sep 24;378(9797):1139-65.

With 4 years until 2015, it is essential to monitor progress towards Millennium Development Goals (MDGs) 4 and 5. Although estimates of maternal and child mortality were published in 2010, an update of estimates is timely in view of additional data sources that have become available and new methods developed. The aim of Lozano and colleagues was to **update previous estimates of maternal and child mortality using better data and more robust methods** to provide the best available evidence for tracking progress on MDGs 4 and 5. They **update the analyses of the progress towards MDGs 4 and 5 from 2010 with additional surveys, censuses, vital registration, and verbal autopsy data**. For children, they estimate **early neonatal** (0-6 days), **late neonatal** (7-28 days), **postneonatal** (29-364 days), **childhood** (ages 1-4 years), and under-5 mortality. They use an improved model for estimating mortality by age under 5 years. For maternal mortality, their updated analysis includes greater than 1000 additional site-years of data. They tested a large set of alternative models for maternal mortality; they used an ensemble model based on the models with the best out-of-sample predictive validity to generate new estimates from 1990 to 2011. **Under-5 deaths have continued to decline, reaching 7.2 million in 2011 of which 2.2 million were early neonatal, 0.7 million late neonatal, 2.1 million postneonatal, and 2.2 million during childhood (ages 1-4 years)**. Comparing rates of decline from 1990 to 2000 with 2000 to 2011 shows that **106 countries have accelerated declines in the child mortality rate in the past decade. Maternal mortality has also continued to decline from 409,100 (uncertainty interval 382,900-437,900) in 1990 to 273,500 (256,300-291,700) deaths in 2011**. They estimate that 56,100 maternal deaths in 2011 were HIV-related deaths during pregnancy. Based on recent trends in developing countries, **31 countries will achieve MDG 4, 13 countries MDG 5, and nine countries will achieve both**. Even though progress on reducing maternal and child mortality in most countries is

accelerating, **most developing countries will take many years past 2015 to achieve the targets** of the MDGs 4 and 5. Similarly, although there continues to be **progress on maternal mortality the pace is slow, without any overall evidence of acceleration**. Immediate concerted action is needed for a large number of countries to achieve MDG 4 and MDG 5.

Abstract : <http://www.ncbi.nlm.nih.gov/pubmed/21937100>

Editor's note: This article provides an update on the maternal mortality estimates provided by Hogan et al in HIV This Week Issue #81, along with progress on under-5 mortality. Although UNFPA has said 'make each and every person count', many countries have weak vital registration systems and health indicator tracking capacity. The ambitious targets of Millennium Development Goal 4 (reduce the under-5 mortality rate by two-thirds between 1990 and 2015) and Goal 5 (reduce the maternal-mortality ratio by three-quarters from 1990 and 2015) require measurement so that lessons can be learned from countries that are on track, resources can be mobilised, and adjustments can be made by countries that are lagging behind to spur the speed of their progress. The high-level Commission on Information and Accountability for Women's and Children's Health recommended that by 2015 'all countries have taken significant steps to establish a system for registration of births, deaths, and causes of death, and have well-functioning health information systems that combine data from facilities, administration services, and surveys'. In the interim, we have to rely on modelling-derived estimates that have varying degrees of uncertainty, depending on the strength of the available data to be entered into the models, among other factors. As well, there may be differences in what to track: HIV-associated maternal deaths or HIV-related maternal deaths. The Global Plan aims to achieve a 50% reduction in the number of HIV-associated deaths during pregnancy, delivery, and the puerperium by 2015. The UNAIDS Terminology Guidelines

www.unaids.org/en/media/unaids/contentassets/documents/document/2011/20111025_UNAIDS_Terminology_Guidelines_En.pdf define HIV-associated deaths as deaths to women with HIV infection during pregnancy, delivery, or the puerperium, including direct maternal deaths to women who are HIV-positive, indirect maternal deaths aggravated by HIV, and HIV-related deaths to women during pregnancy, delivery, or puerperium. These authors define direct and indirect obstetric deaths as all maternal deaths minus the HIV-related deaths during pregnancy so the progress reported here may or may not mirror progress in the HIV-associated maternal mortality that the Global Plan is tracking.

13. Injecting drug use

'It's risky to walk in the city with syringes': understanding access to HIV/AIDS services for injecting drug users in the former Soviet Union countries of Ukraine and Kyrgyzstan

Spicer N, Bogdan D, Brugha R, Harmer A, Murzalieva G, Semigina T. Global Health. 2011 Jul 13;7(1):22.

Despite massive scale up of funds from global health initiatives such as the Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund), **the ambitious target agreed by G8 leaders in 2005 in Gleneagles to achieve universal access to HIV treatment by 2010 has not been reached**. Significant barriers to access remain in former Soviet Union countries, a region now recognised as a priority area by policymakers. There have been few empirical studies of access to HIV services in former Soviet Union countries, resulting in limited understanding and implementation of accessible HIV programmes. This study explores the **multiple access barriers to HIV services experienced by a key risk group – people who inject drugs**. Semi-structured interviews were conducted in two former Soviet Union countries – **Ukraine and Kyrgyzstan** – with clients receiving Global Fund-supported services (Ukraine n=118, Kyrgyzstan n=84), service providers (Ukraine n=138, Kyrgyzstan n=58) and a purposive sample of national and subnational stakeholders (Ukraine n=135, Kyrgyzstan n=86). Systematic content analyses of these qualitative data were conducted by country teams, and a comparative synthesis of findings undertaken by the authors. **Stigmatisation of HIV and drug use was the most important barrier to people who inject drugs accessing HIV services in both countries**. Other connected barriers included: **criminalisation of drug use; discriminatory practices among government service providers; limited knowledge of HIV, services and entitlements; shortages of commodities and human resources; and organisational, economic and geographical barriers**. Approaches to thinking about universal access frequently assume increased availability of services means increased

accessibility of services. This study by Spicer and colleagues demonstrates that **while there is greater availability of HIV services in Ukraine and Kyrgyzstan, this does not equate with greater accessibility** because of multiple, complex, and interrelated barriers to HIV service utilisation at the service delivery level. Factors external to, as well as within, the health sector are key to understanding the access deficit in the former Soviet Union where low or concentrated HIV epidemics are prevalent. **Funders of HIV programmes need to consider how best to tackle key structural and systemic drivers of access including prohibitionist legislation on drugs use, limited transparency and low staff salaries within the health sector.**

Abstract: <http://www.ncbi.nlm.nih.gov/pubmed/21752236>

Editor's note: This snapshot in time of the barriers to access to HIV prevention, treatment, care and support services in the Ukraine and Kyrgyzstan provides one of the clearest views of the difference between availability of services and accessibility to services. Easy-to-reach groups and urban populations have been prioritised in response to the need to demonstrate rapid results for continued performance-based funding by funders and, as a result, these were the settings for this study. In the Ukraine, interviews were conducted in the capital Kyiv, the high prevalence city of Odessa, and the low prevalence city of L'viv. In Kyrgyzstan, the study sites were in the capital Bishkek, the high prevalence cities of Osh and Jalalabad, and the low prevalence city of Karakol. The study found that multiple, complex, interrelated barriers both obstruct access and deter service use. First and foremost is criminalisation of people who inject drugs, resulting in widespread police intimidation, discriminatory practices by service providers, and community-level stigmatisation of drug use. Disincentives to returning used injecting equipment include arrests for 'illegal storage' of drugs in used syringes, thus the title of this article. Everyone involved with harm reduction programmes in any country will gain insights into why access does not simply mean commodity delivery and service coverage, the more easily measured performance indicators. The Vienna Declaration launched in 2010 at the International AIDS Conference to emphasise that drug policy should be based on evidence not ideology remains highly relevant as we enter 2012. You can find it at: <http://www.viennadeclaration.com>

14. Early infant diagnosis

Early infant HIV-1 diagnosis programmes in resource-limited settings: opportunities for improved outcomes and more cost-effective interventions

Ciaranello AL, Park JE, Ramirez-Avila L, Freedberg KA, Walensky RP, Leroy V. BMC Med. 2011 May 20;9:59.

Early infant diagnosis of HIV-1 infection confers substantial benefits to HIV-infected and HIV-uninfected infants, to their families, and to programmes providing prevention of mother-to-child transmission services, but has been challenging to implement in resource-limited settings. **In order to correctly inform parents/caregivers of infant infection status and link HIV-infected infants to care and treatment**, a 'cascade' of events must successfully occur. **A frequently cited barrier to expansion of early infant diagnosis programmes is the cost of the required laboratory assays.** However, substantial implementation barriers, as well as personnel and infrastructure requirements, exist at each step in the cascade. In this update, Ciaranello and colleagues review challenges to uptake at each step in the early infant diagnosis cascade, highlighting that **even with the highest reported levels of uptake, nearly half of HIV-infected infants may not complete the cascade successfully.** They next synthesize the available literature about the costs and cost effectiveness of early infant diagnosis programmes; identify areas for future research; and place these findings within the context of the benefits and challenges to early infant diagnosis implementation in resource-limited settings.

Abstract: <http://www.ncbi.nlm.nih.gov/pubmed/21599888>

Editor's note: This excellent review summaries succinctly the challenges at each step of the early infant diagnosis cascade, from infant presentation for care, the offer of testing, parent/caregiver acceptance of testing, specimen processing, return of results to health care facilities, receipt of results by parents/caregivers, and linkage to care and treatment. WHO recommends that all children under 24 months of age who have proven HIV infection should be started on antiretroviral therapy – and studies

have shown that the earlier the better. Diagnosis of true HIV infection, rather than detection of maternal antibodies, requires virological tests that can detect whether the virus itself is present or not. Infants of mothers not known to have HIV infection will be missed unless testing can be routinely offered to all infants in high prevalence settings. If that first test is an antibody test that comes up positive, then a virological test, such as a DNA PCR (polymerase chain reaction) test that gives qualitative yes/no results or a quantitative RNA PCR test, can diagnose actual HIV infection. Dried blood spot specimens—blood obtained through heel stick and dried on filter paper—are easily and cheaply transported because they are non-infectious and heat-stable. They work for the PCR tests and for p24 antigen tests that detect the viral capsid. But what is really needed is a point-of-care test that would cut the cascade losses due to loss of specimens, slow delivery of results, and unreliable timing for availability of results for parents/caregivers. Reports at the recent ICASA regional conference in Addis Ababa suggest that we will not have long to wait. In the meantime, if you want to understand these early infant diagnostic tests better, you can go to the WHO website to read: http://whqlibdoc.who.int/publications/2010/9789241599085_eng.pdf

15. People living with HIV

HIV infection and mental health: suicidal behaviour—systematic review

Catalan J, Harding R, Sibley E, Clucas C, Croome N, Sherr L. *Psychol Health Med*. 2011 Oct;16(5):588-611.

Suicide has long been associated with serious illness generally and HIV specifically. New treatments have affected prognosis in HIV positively, but it is unclear how they affect **suicidal burden (thoughts, self-harm and completions)**. This review examines all published suicide and HIV data for a definitive account of (1) prevalence of HIV-related suicidality, (2) measurement within studies and (3) effectiveness of interventions. Standard systematic research methods were used to gather quality published papers on HIV and suicide, searching published databases according to quality inclusion criteria. From the search, 332 papers were generated and hand searched resulting in 66 studies for analysis. Of these, **75% were American/European**, but there was representation from developing countries. The breakdown of papers provided 12, which measured completed suicides (death records), five reporting suicide as a cause of attrition. Deliberate self-harm was measured in 21, using 22 instruments; 16 studies measured suicidal ideation using 14 instruments, suicidal thoughts were measured in 17, using 15 instruments. Navigating the diverse range of studies clearly points to a high-suicidal burden among people with HIV. The overview shows that **autopsy studies reveal 9.4% of deceased HIV+ individuals had committed suicide; 2.4% HIV+ study participants commit suicide; approximately 20% of HIV+ people studied had deliberately harmed themselves; 26.9% reported suicidal ideation, 28.5% during the past week and 6.5% reported ideation as a side effect to medication; 22.2% had a suicide plan; 19.7% were generally “suicidal” (11.7% of people with AIDS, 15.3% at other stages of HIV); 23.1% reported thoughts of ending their own life; and 14.4% expressed a desire for death**. Only three studies recruited over 70% female participants (39 studies recruited over 70% men), and six focussed on people who inject drugs. Only three studies looked at interventions – predominantly indirect. Catalan and colleagues’ detailed data suggest that all aspects of suicide are elevated and urgently require **routine monitoring and tracking as a standard component of clinical care**. There is scant evidence of **direct interventions to reduce any aspect of suicidality**, which needs urgent redress.

Abstract: <http://www.ncbi.nlm.nih.gov/pubmed/21745024>

Editor’s note: This systematic review of suicidality among people living with HIV found clear gaps in the research database. Only 25% of the studies were from outside the USA, Canada, and Western Europe and only 1% were from sub-Saharan Africa, the region most affected by HIV. Further, there are no standardised definitions of suicidal ideation, suicidal thoughts, and deliberate self-harm, and a wide range of study instruments exists, making it impossible to pool data or compare findings from different studies. What is clear from the literature is that people living with HIV experience higher levels of suicidality, both before and after HIV diagnosis, and the direction of the relationship between HIV serostatus and suicidality is unclear, meaning that we don’t have good evidence to show us which comes first. Further, it is unclear whether the advent of effective antiretroviral therapy has influenced

levels of suicidality. More research in low- and middle-income countries and more studies of women are urgently needed. From a direct prevention perspective, health care providers should assess for the presence of suicidal thoughts, active plans, and acts of deliberate self-harm in patients living with or at risk for HIV infection. Critically, there is a striking dearth of information on strategies to reduce suicidality among people living with HIV, an area of obvious concern.

16. Sex work

Socio-demographic characteristics and behavioural risk factors of female sex workers in sub-Saharan Africa: a systematic review

Scorgie F, Chersich MF, Ntaganira I, Gerbase A, Lule F, Lo YR. AIDS Behav. 2011 Jul 13.

Sex work remains an important contributor to HIV transmission within early, advanced and regressing epidemics in sub-Saharan Africa, but its social and behavioural underpinnings remain poorly understood, limiting the impact of HIV prevention initiatives. This article systematically reviews the socio-demographics of female sex workers in this region, their **occupational contexts** and **key behavioural risk factors for HIV**. In total 128 relevant articles were reviewed following a search of Medline, Web of Science and Anthropological Index. Female sex workers commonly have **limited economic options, many dependents, marital disruption, and low education**. Their **vulnerability to HIV**, heightened among young women, is inextricably linked to the **occupational contexts of their work**, characterized most commonly by **poverty, endemic violence, criminalisation, high mobility and hazardous alcohol use**. These, in turn, **predict behaviours** such as low condom use, anal sex and co-infection with other sexually transmitted infections. Sex work in Africa cannot be viewed in isolation from other HIV-risk behaviours such as multiple concurrent partnerships—there is often much **overlap between sexual networks**. High turn-over of female sex workers, with **sex work duration typically around 3 years**, further heightens risk of HIV acquisition and transmission. Tailored services at sufficiently high coverage, taking into account the behavioural and social vulnerabilities described here, are urgently required to address the disproportionate burden of HIV carried by female sex workers on the continent.

Abstract: <http://www.ncbi.nlm.nih.gov/pubmed/21750918>

Editor's note: This exhaustive review examines the structural and occupational contexts that shape sex worker vulnerability to HIV exposure in sub-Saharan Africa. It distinguishes between sex work and more 'socially accepted' transactional sex (exchanges of material goods—such as food, cosmetics, transport, school fees, items for children, or a place to sleep for sex). Sex work is defined using the 2000 UNAIDS definition as 'any agreement between two or more persons in which the objective is exclusively limited to the sexual act and ends with that and which involves preliminary negotiations for a price'. Sex work in sub-Saharan Africa is not typically based in large-scale brothels, as are found in Asia, and does not commonly involve intermediaries, although there are pimps in some settings and middlemen on the highways. The settings for solicitation are at the place of sex, e.g. outdoors in some settings, or different from the place of sex, e.g. sex may be negotiated in a drinking venue but take place at the sex worker's home. As virtually everywhere worldwide, sex in the man's space, e.g. his car or room, entails increased risk of violence and forced unprotected sex. Overall, clients come from all corners of society. Although mobility, employment in seasonal agriculture or the military, and separation of workers from family are factors that predict purchase of sexual services, frequently men residing in surrounding communities are also clients. Condom use, anal and oral sex practices, alcohol and other substance use, harmful legislation, human rights violations, coercion, stigma, and poor access to services—you will find them all mentioned in this review. The challenge is to move from epidemiological studies that treat sex workers as a 'core group' to implementation of rights-based, evidence-informed initiatives that are designed for and by sex workers to reduce vulnerability by improving sex work conditions and contexts. This would be greatly facilitated by structural interventions to decriminalise sex work, as Senegal has done.

17. Prisons

Limited access to HIV prevention in French prisons (ANRS PRI2DE): implications for public health and drug policy

Michel L, Jauffret-Roustide M, Blanche J, Maguet O, Calderon C, Cohen J, Carrieri PM; ANRS PRI²DE study group. *BMC Public Health*. 2011 May 27;11:400.

Overpopulation, poor hygiene and disease prevention conditions in prisons are major structural determinants of increased infectious risk within prison settings but evidence-based national and WHO guidelines provide clear indications on how to reduce this risk. Michel and colleagues sought to estimate the level of infectious risk by **measuring how French prisons adhere to national and WHO guidelines**. A nationwide survey targeting the heads of medical (all French prisons) and psychiatric (26 French prisons) units was conducted using a postal questionnaire and a phone interview mainly focusing on **access to prevention interventions**, i.e. **bleach, opioid substitution treatment, HBV vaccination and post-exposure prophylaxis for French prisoners**. Two scores were built reflecting adherence to national and WHO international guidelines, ranging from 0 (no adherence) to 10 (maximum adherence) and 0 to 9 respectively. A majority (N = 113 (**66%**)) of the **171 prisons answered the questionnaires, representing 74% coverage (46,786 prisoners) of the French prison population**: 108 were medical units and 12 were psychiatric units. Inmate access to prevention was poor. The median[IQR] score measuring **adherence to national guidelines was quite low (4.5[2.5; 5.5]) but adherence to WHO guidelines was even lower 2.5[1.5; 3.5]**; post-exposure prophylaxis was absent despite reported risky practices. **Unsuitable opioid substitution treatment delivery practices were frequently observed**. A wide gap exists between HIV prevention policies and their application in prisons. **Similar assessments in other countries may be needed to guide a global policy reform in prison settings**. Adequate funding together with innovative interventions able to remove structural and ideological barriers to HIV prevention are now needed to motivate those in charge of prison health, to improve their working environment and to relieve French prisoners from their currently debilitating conditions.

Abstract: <http://www.ncbi.nlm.nih.gov/pubmed/21619573>

Editor's note: Prison populations in France have increased by one-third in the last 10 years, partly due to the criminalisation of drug use. In addition to creating over-population of prisons, criminalisation of drug use is a barrier to implementation of effective harm reduction programmes both in the community and in prisons. Needle syringe programmes are underway in more than 50 prisons in 12 countries, but France is not one of them. Condoms are available in prisons in many countries, the USA being a notable exception at less than 1% of prisons, but they are not always accessible with anonymity. Although 95% of the French prisons in this study report that condoms are available, for the most part this is only in medical units so French prisons score 9% and 12% on adherence to national and WHO/UNAIDS/UNODC guidelines on condom access, respectively. The lesson learned is that countries should measure their performance in prison settings against national and international standards and then design implementation plans to address the shortfall and do so rapidly. Most prisoners are eventually released back into the community—there is a tangible opportunity that should not be missed, while they are captive, to equip them to be purveyors of positive messages about HIV prevention, testing, stigma, treatment adherence, and support to others.

That was **HIV This Week**, signing off.

Editors' notes on journal access

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