Welcome to the 79th issue of *HIV This Week*! In this issue, we cover the following topics:

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2. **Test and treat**
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3. **Maternal mortality**
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15. **Structural interventions**
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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](http://www.unaids.org).
1. Alcohol and unsafe sex

Causal links between binge drinking patterns, unsafe sex and HIV in South Africa: its time to intervene.


South Africa has a massive burden of HIV and alcohol disease, and these pandemics are inextricably linked. Much evidence indicates that alcohol independently influences decisions around sex, and undermines skills for condom negotiation and correct use. Thus, not surprisingly, people with problem drinking in Africa have twofold higher risk for HIV than non-drinkers. Also, sexual violence incidents often coincide with heavy alcohol use, both among perpetrators and victims. Reducing alcohol harms necessitates both population- and individual-level interventions, especially raised taxation, regulation of alcohol advertising and provision of Brief Interventions. Alcohol counselling interventions must include discussion of linkages between alcohol and sex, and consequences thereof. Within positive-prevention services, alcohol reduction interventions could diminish HIV transmission. A trial is needed to definitively demonstrate that reduced drinking lowers HIV incidence. However, given available evidence, implementation of effective interventions could alleviate much alcohol-attributable disease, including unsafe sex, sexual violence, unintended pregnancy and, likely, HIV transmission.

For abstract access click here: http://ijsa.rsmjournals.com/cgi/content/full/21/1/2

Editor's note: With the annual costs of direct alcohol harm in South Africa estimated at 1% of the gross domestic product, alcohol accounting for 7.9% of disease burden (almost double alcohol’s global burden of disease of 4%), and the causal pathway between alcohol use and HIV acquisition broadly accepted, HIV prevention programming clearly should include campaigns against alcohol-related harm. The 8 effective strategies described here are: raising awareness and political commitment, community action to reduce harmful use, health-sector response, drink-driving policies and countermeasures, reducing the availability of alcohol, addressing alcoholic beverage marketing, modifying pricing policies, and regulating the drinking context. These are all structural interventions, with the exception of the health sector response. It focuses on provider-initiated screening, like provider-initiated HIV testing and counselling, to identify people in need of prevention interventions to reduce consumption or treatment for alcohol dependence. These strategies can help the estimated 1 in 5 people living with HIV who are alcohol dependent as well as HIV-negative individuals for whom alcohol consumption can lead to regretted sexual relations, inconsistent condom use, condom accidents, and increased incidence of sexually transmitted infections. When addressing HIV and/or alcohol harm, both individual and structural interventions are critical – and there are strong arguments for including alcohol-reduction programmes in combination prevention in many contexts worldwide.

2. Test and treat

Examining the promise of HIV elimination by 'test and treat' in hyperendemic settings.

Dodd PJ, Garnett GP, Hallett TB. AIDS. 2010 Feb 11. [Epub ahead of print]

It has been suggested that a new strategy for HIV prevention, 'Universal Test and Treat', whereby everyone is tested for HIV once a year and treated immediately with antiretroviral therapy if they are infected, could 'eliminate' the epidemic and reduce antiretroviral therapy costs in the long term. The authors investigated the impact of test-and-treat interventions under a variety of assumptions about the epidemic using a deterministic mathematical model. Their model shows that such an intervention can substantially reduce HIV transmission, but that impact depends crucially on the epidemiological context; in some situations, less aggressive interventions achieve the same results, whereas in others, the proposed intervention reduces HIV by much less. It follows that testing every year and treating immediately is not necessarily the most cost-efficient strategy. Dodd and colleagues also show that a test-and-treat intervention that does not reach full implementation or coverage could, perversely, increase long-term antiretroviral therapy costs. Interventions that prevent new infections through antiretroviral
therapy scale-up may hold substantial promise. However, as plans move forward, careful consideration should be given to the nature of the epidemic and the potential for perverse outcomes.

For abstract access click here:

Editors’ note: This modelling analysis highlights three important aspects of ‘test and treat’ strategies that require thoughtful consideration. The first is epidemic context and, in particular, the properties of the sex partner network (heterogeneity, concurrency, and mixing) that can influence the impact of a ‘test and treat’ approach. The second is the diminishing returns of yearly testing – this modelling suggests that testing everyone every 3 to 5 years appears most cost-efficient, depending on the epidemic context, life expectancy, and the costs of testing and treatment. The third is the dramatic spiralling in treatment costs that is likely if testing is not frequent enough and treatment coverage is suboptimal. These qualitative insights are helpful and they show that we need more evidence to inform the modelling. There is no doubt that the science underpinning ‘test and treat’ is promising: viral load drops in individuals placed on antiretroviral treatment and reduced transmission in discordant couple studies. Policy makers need the results of clinical trials, such as HPTN 052, and community impact evaluations such as the British Columbia Seek and Treat pilot project and the NIH Test and Treat feasibility assessments in Washington and the Bronx, to inform policy and programming. In the meantime, millions of people in need of treatment now, whether defined by the old under 200 CD4+ count criterion or the new under 350 CD4+ cell count guidelines, will die if we don’t get treatment to them urgently.

3. Maternal mortality

Mortality among HIV-positive postpartum women with high CD4 cell counts in Zimbabwe.

Hargrove J, Humphrey J, for the ZVITAMBO Study Group. AIDS. 2010. 24:F11–F14

Whereas antiretroviral treatment initiated at CD4 cell counts 351–450 cells/ml reduces mortality, compared with starting at lower CD4 levels, there is currently no evidence for the advantages of initiating treatment at CD4 cell counts greater than 450 cells/ml. Mortality hazard, as a function of CD4 cell count, was estimated among postpartum HIV-positive women in Zimbabwe, using HIV-negative women as the reference group. Mortality within 24 months postpartum was 54 times higher among women with CD4 cell counts less than 200 cells/ml, fell to 5.4 times higher for those with CD4 cell counts 400–600 cells/ml but fell little thereafter. For CD4 cell counts greater than 600 cells/ml the hazard was 6.2 (95% confidence interval 3.2–11.9). Early antiretroviral therapy initiation for all HIV-positive pregnant women may benefit individual mothers and infants, and simultaneously reduce population HIV incidence.

For abstract access click here:

Editors’ note: The striking findings in this study that enrolled 14,110 postpartum women within 96 hours of delivery to a vitamin A supplementation trial call into question the new World Health Organisation (WHO) adult treatment guidelines. The guidelines recommend that antiretroviral therapy be provided for all HIV-infected pregnant women with CD4 cell counts <350 cells/mm³, irrespective of WHO clinical staging, and for all HIV-infected pregnant women in WHO clinical stage 3 or 4, irrespective of CD4 cell count. This study found a higher risk of mortality for HIV-positive women in the 24 months following delivery across the entire CD4 cell count distribution spectrum compared to HIV-negative women. Although evidence suggests that pregnancy does not accelerate HIV disease progression beyond the passage of 9 months of time, most of the data come from industrialised settings. In contrast, these Zimbabwean findings suggest that serious
consideration should be given to starting all pregnant women with HIV infection on antiretroviral treatment for life, regardless of CD4+ count.

4. Cost effectiveness

Cost-effectiveness of routine rapid human immunodeficiency virus antibody testing before DNA-PCR testing for early diagnosis of infants in resource-limited settings.


Infants born to HIV-infected women should receive HIV testing to allow early diagnosis and treatment. Recommendations for resource-limited settings stress laboratory-based virologic assays. While effective, these tests are logistically complex and expensive. This study explored the cost-effectiveness of incorporating initial screening with rapid HIV tests into the conventional testing algorithm to screen-out HIV-uninfected infants, thereby reducing the need for costly virologic testing. Data on HIV prevalence, rapid HIV tests sensitivity and specificity, and costs were collected from 820 HIV-exposed children (1.5-18 months) attending 2 postnatal screening programs in Uganda during July 2005 to December 2006. Cost-effectiveness models compared the conventional testing algorithm DNA polymerase chain reaction (DNA-PCR with Roche Amplicor v1.5) with a modified algorithm (initial rapid HIV tests to screen-out HIV-uninfected infants before DNA-PCR). The model estimated that the conventional algorithm would identify 94.3% (91.8%-94.7%) of HIV-infected infants, compared with 87.8% (79.4%-90.5%) for a modified algorithm using rapid HIV tests (HIV 1/2 Determine) and excluding the need for DNA-PCR for HIV antibody-negative infants. Costs per infant were $23.47 ($23.32-$23.76) for the conventional algorithm and between $22.75 ($21.89-$23.31) and $7.58 ($6.41-$10.75) for the modified algorithm, depending on infant age and symptoms. Compared with the conventional algorithm, costs per HIV-infected infant identified using the modified algorithm were higher in 1.5-to 3-month-old infants, but significantly lower in 3-month-old and older infants. Models replicating the whole infant testing program showed the modified algorithm would have marginally lower sensitivity, but would reduce total program costs by 27% to 40%, producing an incremental cost-effectiveness ratio of $1489 ($686-$6781) for the conventional versus modified algorithms. Screening infants with rapid HIV tests before DNA-PCR is cost-effective in infants 3 months old or older. Incorporating rapid HIV tests into early infant testing programs could improve cost-effectiveness and reduce program costs.

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Editors’ note: In the absence of antiretroviral prophylaxis, between 70 and 85% of infants born to mothers with HIV infection do not acquire HIV during pregnancy, labour, and delivery. However, all infants born to such mothers will have a positive HIV antibody test because their mother’s HIV antibodies cross the placenta before birth and persist in the baby’s blood up to 18 months of age. Because parents want to know whether their baby is infected and because antiretroviral treatment should be started in infants as soon as HIV infection is detected, it is not acceptable to wait until 18 months of age for a negative HIV antibody test to confirm that the baby has no antibodies of its own. Current policy in Uganda recommends testing of all HIV-exposed infants at 10 weeks of age, at their second immunization visit, by DNA-PCR which detects the virus itself, not antibodies. Although cost-effectiveness studies such as this one are context-specific with results varying by HIV prevalence, costs of supplies and personnel, equipment, etc., they are nonetheless of interest for programme planners in similar settings. The idea of using a rapid test to screen out infants that are likely not infected and then use the DNA-PCR test only on those that are rapid test-positive is partly motivated by the cost and complexity of DNA-PCR testing and partly by an appreciation of the visit burden imposed on parents by repeated testing visits should the first DNA-PCR be negative and the baby continues to breastfeed. Given that the algorithm studied here was cost-effective only in infants 3 months or older, there is not much to suggest that Uganda should
change its current 10-week DNA-PCR testing policy. Using a rapid test to screen above that age in breastfeeding infants in order to decide whether a DNA-PCR should be done could be considered.


HIV incidence was substantially lower among circumcised versus uncircumcised heterosexual African men in three clinical trials. Based on those findings, the authors modelled the potential effect of newborn male circumcision on a U.S. male’s lifetime risk of HIV, including associated costs and quality-adjusted life-years saved. Given published estimates of U.S. males’ lifetime HIV risk, they calculated the fraction of lifetime risk attributable to heterosexual behaviour from 2005-2006 HIV surveillance data. They assumed 60% efficacy of circumcision in reducing heterosexually-acquired HIV over a lifetime, and varied efficacy in sensitivity analyses. They calculated differences in lifetime HIV risk, expected HIV treatment costs and quality-adjusted life years (QALYs) among circumcised versus uncircumcised males. The main outcome measure was cost per HIV-related QALY saved. Circumcision reduced the lifetime HIV risk among all males by 15.7% in the base case analysis, ranging from 7.9% for white males to 20.9% for black males. Newborn circumcision was a cost-saving HIV prevention intervention for all, black, and Hispanic males. The net cost of newborn circumcision per QALY saved was $87,792 for white males. Results were most sensitive to the discount rate, and circumcision efficacy and cost. Newborn circumcision resulted in lower expected HIV-related treatment costs and a slight increase in QALYs. It reduced the 1.87% lifetime risk of HIV among all males by about 16%. The effect varied substantially by race and ethnicity. Racial and ethnic groups who could benefit the most from circumcision may have least access to it due to insurance coverage and state Medicaid policies, and these financial barriers should be addressed. More data on the long-term protective effect of circumcision on heterosexual males as well as on its efficacy in preventing HIV among men who have sex with men would be useful.

For full text access click here:
http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0008723

Editors’ note: This cost-effectiveness analysis in the USA, which assessed the impact of infant male circumcision programmes on the lifetime HIV risk from heterosexual contact, found that African American and Hispanic males would benefit most from newborn circumcision. They have a higher lifetime risk of HIV, a higher risk of acquiring through heterosexual contact (6.2% for black males versus 0.94% for white males), and lower adult male circumcision prevalence. Although 88% of white males are circumcised, this figure falls to 73% among black males, and 42% among Hispanic males. However, these very populations are often least likely, on financial and insurance coverage grounds, to be able to obtain newborn circumcision in the current US health care system should they decide to circumcise their male infants on health grounds. These include reduced risk of some sexually transmitted infections, infant urinary tract infections, penile cancer and cervical cancer in female partners. Cost-effectiveness analysis can inform decision-making when conditions for implementation are in place. In this case, the long road to health care reform in the USA has possibly been a major factor delaying policy change on infant male circumcision in the USA.

5. Treatment

Economic and quality of life outcomes of antiretroviral therapy for HIV/AIDS in developing countries: a systematic literature review.

The impacts of antiretroviral therapy on quality of life, mental health, labour productivity, and economic wellbeing for people living with HIV in developing countries are only beginning to be measured. The authors conducted a systematic literature review to analyze the effect of antiretroviral therapy on these economic and quality of life indicators in developing countries and
assess the state of research on these topics. They searched Ovid/Medline, PubMed, Psych Info, Web of Science, Google Scholar, and the abstract database of the International AIDS Society Conference and the Conference on Retroviruses and Opportunistic Infections. Both qualitative and quantitative studies were included, as were peer-reviewed articles, gray literature, and conference abstracts and presentations. Findings are reported from 21 publications, including 14 full-length articles, six abstracts, and one presentation (representing 16 studies). Compared to HIV-positive patients not yet on treatment, patients on antiretroviral therapy reported significant improvements in physical, emotional and mental health, and daily function. Work performance improved and absenteeism decreased, with the most dramatic changes occurring in the first three months of treatment and then levelling off. Little research has been done on the impact of antiretroviral treatment on household wellbeing, with modest changes in child and family wellbeing within households where adults are receiving antiretroviral therapy reported so far. Most studies from developing countries have not yet assessed economic and quality of life outcomes of therapy beyond the first year; therefore, longitudinal outcomes are still unknown. Findings were limited geographically, with an emphasis on sub-Saharan Africa and adult treatment. As antiretroviral therapy roll out extends throughout high HIV prevalence, low-resource countries and is sustained over years and decades, research on paediatric and differential gender economic and quality of life outcomes will become increasingly urgent, as will systematic evaluation of antiretroviral therapy programs.

For full text access click here:
http://www.informaworld.com/smpp/content~db=all?content=10.1080/09540120902889926

Editors’ note: Quality of life is defined in the John Last Dictionary of Epidemiology as the degree to which persons perceive themselves able to function physically, emotionally, and socially. People living with HIV who adhere to treatment show quick rises in CD4+ counts and drops in viral loads to undetectable levels within a year. This review of the literature, focused on low- and middle-income countries, found increases in emotional wellbeing even among people accepted for treatment who had not yet started it. Initiation of antiretroviral therapy was associated with reduced anxiety, depression, and dementia, as well as reduced absenteeism and increased productivity and work performance. When adults were better able to work, child labour fell and wasting in children under 5 decreased while school enrolment and family nutrition increased. Further studies, qualitative and longitudinal, are needed to track whether there is a shift from treatment optimism to treatment fatigue and declining quality of life over time. Adherence to drug treatment for life clearly plays a key role as poor treatment adherence can undermine quality of life while poor quality of life makes treatment adherence less likely.

Seven-year experience of a primary care antiretroviral treatment programme in Khayelitsha, South Africa.


Boulle et al report on outcomes after 7 years of a community-based antiretroviral therapy programme in Khayelitsha, South Africa, with death registry linkages to correct for mortality under-ascertainment. This is an observational cohort study. Since inception, patient-level clinical data have been prospectively captured on-site into an electronic patient information system. Patients with available civil identification numbers who were lost to follow-up were matched with the national death registry to ascertain their vital status. Corrected mortality estimates weighted these patients to represent all patients lost to follow-up. CD4 cell count outcomes were reported conditioned on continuous virological suppression. Seven thousand, three hundred and twenty-three treatment-naive adults (68% women) started antiretroviral therapy between 2001 and 2007, with annual enrolment increasing from 80 in 2001 to 2087 in 2006. Of 9.8% of patients lost to follow-up for at least 6 months, 32.8% had died. Corrected mortality was 20.9% at 5 years (95% confidence interval 17.9-24.3). Mortality fell over time as patients accessed care earlier (median CD4 cell count at enrolment increased from 43 cells/mul in 2001 to 131 cells/mul in 2006). Patients who remained virologically suppressed continued to gain CD4 cells at 5 years (median 22 cells/mul per 6 months). By 5 years, 16.0% of patients had failed virologically and
12.2% had been switched to second-line therapy. At a time of considerable debate about future global funding of antiretroviral therapy programmes in resource-poor settings, this study has demonstrated substantial and durable clinical benefits for those able to access antiretroviral therapy throughout this period, in spite of increasing loss to follow-up.

For abstract access click here:

Editors’ note: The flagship Khayelitsha HIV treatment programme was one of the very first programmes to demonstrate through a pilot demonstration project the feasibility of antiretroviral treatment provision. With the focus of attention now shifted from feasibility to sustainability, the findings from the Khayelitsha antiretroviral treatment programme, which has been run by government health services for the past few years, are enlightening. Almost 80% of patients are alive after 5 years of antiretroviral treatment and, of those tested, 80% are virologically suppressed. Between year 4 and 5 on antiretroviral treatment, CD4+ counts among those who were adherent rose a median of 22 cells/µl per 6-month period. However, almost one in five patients reaching 5 years is on a second-line regimen. As treatment programmes begin to mature, increasing numbers of patients will require timely and justified switches to second-line regimens. This underscores the increasing importance of significant price reductions by manufacturers, whether brand-name or generic, along with other strategies consistent with the Doha Declaration of 2001.

6. Injecting drug use

The Washington Needle Depot: fitting healthcare to injection drug users rather than injection drug users to healthcare: moving from a syringe exchange to syringe distribution model.


Needle exchange programs chase political as well as epidemiological dragons, carrying within them both implicit moral and political goals. In the exchange model of syringe distribution, injection drug users must provide used needles in order to receive new needles. Distribution and retrieval are co-existent in the exchange model. Likewise, limitations on how many needles can be received at a time compel addicts to have multiple points of contact with professionals where the virtues of treatment and detox are impressed upon them. The centre of gravity for syringe distribution programs needs to shift from needle exchange to needle distribution, which provides unlimited access to syringes. This paper provides a case study of the Washington Needle Depot, a program operating under the syringe distribution model, showing that the distribution and retrieval of syringes can be separated with effective results. Further, the experience of injecting drug users is utilized, through paid employment, to provide a vulnerable population of people with clean syringes to prevent HIV and HCV.

For full text access click here: http://www.harmreductionjournal.com/content/7/1/1

Editors’ note: Although NSP or needle-syringe programmes often began on an exchange basis as a means to achieve political buy-in, there are few that have remained so for a variety of reasons. These include the ineffectiveness of the exchange model or of needle quotas in controlling HIV epidemics driven in part by injecting cocaine, which has a short duration of action and tends to be injected frequently when it is being injected. More significantly, a shift in thinking about risk behaviour in general and injecting behaviour more specifically has led to a focus on the risk environment. With respect to people who inject drugs, multi-person use of injecting equipment is more likely when needles and syringes are in short supply. Calling this ‘needle sharing’ implies that this is a positive social behaviour rather than one determined primarily by the availability of equipment. For 9 years after the first needle syringe programmes in Canada opened in Vancouver and Montreal, the Olympic City used an exchange model. Whether this contributed to the extent of the HIV and hepatitis C epidemics in Vancouver today remains a question but since 2000 needle syringe distribution has been decentralised to health clinics, peer support groups, homeless
7. Universal access

Estimation of antiretroviral therapy coverage: methodology and trends.


The purpose of this review was to present the methodology used to calculate coverage of antiretroviral therapy and review global and regional trends in antiretroviral therapy coverage. There has been a steady increase in antiretroviral therapy coverage over the last decade with a more rapid increase in recent years. Current estimates of antiretroviral therapy coverage are 43% for adults and 38% for children (ages 0-14 years). **Methods for calculating coverage rely on good-quality patient monitoring systems in countries**, and well informed models are needed to estimate the number of people in need of treatment. The estimated coverage rates show that antiretroviral therapy programs have improved over the past 8 years; however, **approximately 58% (53-60%) of those people in need of antiretroviral therapy are still not on treatment**. High quality data are needed to accurately measure changes in antiretroviral therapy coverage.

For abstract access click here:


Editors’ note: Antiretroviral treatment coverage is defined as the percentage of people on treatment (the numerator) among those in need of treatment (the denominator). Few countries, notably Brasil and Zambia, have a monitoring system based on individual information. Elsewhere facility-based reporting of aggregated data based on patient and pharmacy monitoring is compiled to produce a national level estimate. In 2008, 91% of 149 low- and middle-income countries reported the number of people on antiretroviral treatment with 70% of those disaggregating data by sex. The estimated 9.5 million (8.6-10 million) people currently in need of antiretroviral treatment will be joined by many million more as countries begin to adopt the new WHO antiretroviral treatment guidelines. Therefore, although the numerator (those on treatment), estimated at over 4 million (3.7-4.4 million) in 2008, is steadily growing, the denominator is set to rise dramatically. Regardless of whether the old or the new denominator or both are used to determine coverage, the focus should be on accelerating the growth of the numerator!

8. Reproductive health

Reproductive choices for women with HIV.


Access to reproductive health services for women with HIV is critical to ensuring their reproductive needs are addressed and their reproductive rights are protected. In addition, preventing unintended pregnancies in women with HIV is an essential component of a comprehensive prevention of mother-to-child transmission (PMTCT) programme. As a result, a call for stronger linkages between sexual and reproductive health and HIV policies, programmes and services has been issued by several international organizations. However, implementers of PMTCT and other HIV programmes have been constrained in translating these goals into practice. The obstacles include: (i) the narrow focus of current PMTCT programmes on treating HIV-positive women who are already pregnant; (ii) separate, parallel funding mechanisms for sexual and reproductive health and HIV programmes; (iii) political resistance from major HIV funders and policy-makers to include sexual and reproductive health as an important HIV programme component; and (iv) gaps in the evidence base regarding effective approaches for integrating sexual and reproductive health and HIV services. However, we now have a new opportunity to address these essential linkages. More supportive political views in...
the United States of America and the emergence of health systems strengthening as a priority global health initiative provide important springboards for advancing the agenda on linkages between sexual and reproductive health and HIV. By tapping into these platforms for advocating and by continuing to invest in research to identify integrated service delivery best practices, we have an opportunity to strengthen ties between the two synergistic fields.

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Editors’ note: This ‘must read’ article cogently lays out the human rights and public health arguments for effective linkages and integration of HIV services with sexual and reproductive services. If you have not been convinced that contraceptive use should be an indicator of programmatic success for vertical transmission prevention programmes, you may think twice after reading this article about measuring only the ‘cascade’ which starts with the proportion of women accessing antenatal care services. Women living with HIV need sexual and reproductive health services when they do not wish to become pregnant, when they wish to become pregnant, when they are pregnant and wish to continue their pregnancy, and when they are pregnant and do not wish to continue their pregnancy. As the Convention on the Elimination of all Forms of Discrimination Against Women states: all women have the right ‘to decide freely and responsibly on the number and spacing of their children and to have access to the information, education, and means to enable them to exercise these rights’. A new wind is blowing and it is high time to make both vertical and integrated sexual and reproductive health services priority strategies as we aim to eliminate mother-to-child HIV transmission.

9. Herpes and HIV

Acyclovir and Transmission of HIV-1 from Persons Infected with HIV-1 and HSV-2.


Most persons who are infected with human immunodeficiency virus type 1 (HIV-1) are also infected with herpes simplex virus type 2 (HSV-2), which is frequently reactivated and is associated with increased plasma and genital levels of HIV-1. Therapy to suppress HSV-2 reduces the frequency of reactivation of HSV-2 as well as HIV-1 levels, suggesting that suppression of HSV-2 may reduce the risk of transmission of HIV-1. Celum et al conducted a randomized, placebo-controlled trial of suppressive therapy for HSV-2 (acyclovir at a dose of 400 mg orally twice daily) in couples in which only one of the partners was seropositive for HIV-1 (CD4 count, >/=250 cells per cubic millimetre) and that partner was also infected with HSV-2 and was not taking antiretroviral therapy at the time of enrolment. The primary end point was transmission of HIV-1 to the partner who was not initially infected with HIV-1; linkage of transmissions was assessed by means of genetic sequencing of viruses. A total of 3408 couples were enrolled at 14 sites in Africa. Of the partners who were infected with HIV-1, 68% were women, and the baseline median CD4 count was 462 cells per cubic millimetre. Of 132 HIV-1 seroconversions that occurred after randomization (an incidence of 2.7 per 100 person-years), 84 were linked within couples by viral sequencing: 41 in the acyclovir group and 43 in the placebo group (hazard ratio with acyclovir, 0.92, 95% confidence interval [CI], 0.60 to 1.41; P=0.69). Suppression with acyclovir reduced the mean plasma concentration of HIV-1 by 0.25 log(10) copies per millilitre (95% CI, 0.22 to 0.29; P<0.001) and the occurrence of HSV-2-positive genital ulcers by 73% (risk ratio, 0.27; 95% CI, 0.20 to 0.36; P<0.001). A total of 92% of the partners infected with HIV-1 and 84% of the partners not infected with HIV-1 remained in the study for 24 months. The level of adherence to the dispensed study drug was 96%. No serious adverse
events related to acyclovir were observed. Daily acyclovir therapy did not reduce the risk of transmission of HIV-1, despite a reduction in plasma HIV-1 RNA of 0.25 log(10) copies per millilitre and a 73% reduction in the occurrence of genital ulcers due to HSV-2.

For abstract access click here:

Editors’ note: Given that the majority of people with HIV infection also have herpes simplex-2 (HSV-2) infection, genital shedding of herpes occurs on up to 30% of days in co-infected people living with HIV even when they have no symptoms, and HSV-2 reactivation without symptoms has been associated with increased HIV viral load in the blood plasma and genital tract, there was good reason to conduct a large trial of serodiscordant couples to see if herpes suppression would reduce HIV transmission. After all, five trials had already shown that daily suppressive therapy for HSV-2 reduced plasma HIV viral load. Of 6543 HIV-discordant couples screened, 3408 were enrolled at 14 sites in Botswana, South Africa, Zambia, Kenya, Rwanda, Tanzania, and Uganda. With adherence to acyclovir/placebo high and HIV infections acquired outside the couple excluded from the final analysis through genotyping to link transmitted viruses, this well-powered trial gave an unequivocal answer. Despite reductions in HIV viral load, acyclovir did not reduce HIV transmission. However, this study documented a 16% reduction in disease progression for those in the acyclovir arm, all of whom started the study with CD4+ counts above 250. This suggests that, for their own health, co-infected people who are not yet eligible for antiretroviral treatment may benefit from daily acyclovir – it is off-patent and cheap and has few side effects.

10. Tuberculosis
Timing of Initiation of Antiretroviral Drugs during Tuberculosis Therapy.

The rates of death are high among patients with coinfection with tuberculosis and the human immunodeficiency virus (HIV). The optimal timing for the initiation of antiretroviral therapy in relation to tuberculosis therapy remains controversial. In an open-label, randomized, controlled trial in Durban, South Africa, Karim et al assigned 642 patients with both tuberculosis and HIV infection to start antiretroviral therapy either during tuberculosis therapy (in two integrated-therapy groups) or after the completion of such treatment (in one sequential-therapy group). The diagnosis of tuberculosis was based on a positive sputum smear for acid-fast bacilli. Only patients with HIV infection and a CD4+ cell count of less than 500 per cubic millimetre were included. All patients received standard tuberculosis therapy, prophylaxis with trimethoprim–sulfamethoxazole, and a once-daily antiretroviral regimen of didanosine, lamivudine, and efavirenz. The primary end point was death from any cause. This analysis compares data from the sequential-therapy group and the combined integrated-therapy groups up to September 1, 2008, when the data and safety monitoring committee recommended that all patients receive integrated antiretroviral therapy. There was a reduction in the rate of death among the 429 patients in the combined integrated-therapy groups (5.4 deaths per 100 person-years, or 25 deaths), as compared with the 213 patients in the sequential-therapy group (12.1 per 100 person-years, or 27 deaths); a relative reduction of 56% (hazard ratio in the combined integrated-therapy groups, 0.44; 95% confidence interval, 0.25 to 0.79; P = 0.003). Mortality was lower in the combined integrated-therapy groups in all CD4+ count strata. Rates of adverse events during follow-up were similar in the two study groups. The initiation of antiretroviral therapy during tuberculosis therapy significantly improved survival and provides further impetus for the integration of tuberculosis and HIV services.

For abstract access click here: http://content.nejm.org/cgi/content/short/362/8/697?ssource=mfv
Editors’ note: Despite WHO guidelines encouraging concomitant treatment of TB and HIV, antiretroviral treatment is often deferred because of worries about possible drug interactions between some antiretroviral drugs and the TB drug rifampin, immune reconstitution inflammatory syndrome (IRIS), adherence concerns because of a high pill burden, and programme challenges of coordinating HIV and TB care. The result is that people with active TB infection who are eligible for antiretroviral treatment may die before they get HIV treatment. The SAPIT (Starting Antiretroviral Therapy at Three Points in Tuberculosis) trial was stopped early by its DSMB (Data Safety Monitoring Board) which recommended that all patients in the sequential-therapy group be started on HIV treatment immediately because of their significantly higher risk of mortality. The results of the other two groups, i.e. those who had started HIV treatment 4 weeks after the start of TB treatment and those who started after 2 months of TB treatment, were combined in this analysis. Whether there are differences between outcomes in these two integrated therapy groups will not be known until the trial ends. In the meantime, the reduced all-cause mortality, improved TB outcomes, and reduced incidence of IRIS found in SAPIT were considered in the development of the new WHO guidelines which recommend that all people with HIV infection who develop active TB should be placed on antiretroviral treatment as soon as possible after their TB treatment has begun. For more information, see http://www.who.int/hiv/pub/arv/advice/en/index.html.


Individuallys with human immunodeficiency virus (HIV) infection are at an increased risk of developing active tuberculosis (TB). It is known that treatment of latent TB infection (LTBI), also referred to as TB preventive therapy or chemoprophylaxis, helps to prevent progression to active disease in HIV-negative populations. However, the extent and magnitude of protection (if any) associated with preventive therapy in those infected with HIV should be quantified. This present study is an update of the original review. The objective of the review was to determine the effectiveness of TB preventive therapy in reducing the risk of active tuberculosis and death in HIV-infected persons. This review was updated using the Cochrane Controlled Trials Register (CCTR), MEDLINE, EMBASE, AIDSLINE, AIDSTRIALS, AIDSsearch, NLM Gateway and AIDSDRUGS (publication date from 01 July 2002 to 04 April 2008). Akolo et al also scanned reference lists of articles and contacted authors and other researchers in the field in an attempt to identify additional studies that may be eligible for inclusion in this review. They included randomized controlled trials in which HIV positive individuals were randomly allocated to TB preventive therapy or placebo, or to alternative TB preventive therapy regimens. Participants could be tuberculosis skin test positive or negative, but without active tuberculosis. Three reviewers independently applied the study selection criteria, assessed study quality and extracted data. Effects were assessed using relative risk for dichotomous data and mean differences for continuous data. 12 trials were included with a total of 8578 randomized participants. TB preventive therapy (any anti-TB drug) versus placebo was associated with a lower incidence of active TB (RR 0.68, 95% CI 0.54 to 0.85). This benefit was more pronounced in individuals with a positive tuberculin skin test (RR 0.38, 95% CI 0.25 to 0.57) than in those who had a negative test (RR 0.89, 95% CI 0.64 to 1.24). Efficacy was similar for all regimens (regardless of drug type, frequency or duration of treatment). However, compared to isoniazid (INH) monotherapy, short-course multi-drug regimens were much more likely to require discontinuation of treatment due to adverse effects. Although there was reduction in mortality with isoniazid monotherapy versus placebo among individuals with a positive tuberculin skin test (RR 0.74, 95% CI 0.55 to 1.00) and with isoniazid plus rifampicin versus placebo regardless of tuberculin skin test status (RR 0.69, 95% CI 0.50 to 0.95), overall, there was no evidence that TB preventive therapy versus placebo reduced all-cause mortality (RR 0.94, 95% CI 0.85 to 1.05). The authors conclude that treatment of latent tuberculosis infection reduces the risk of active TB in HIV-positive individuals especially in those with a positive tuberculin skin test. The choice of regimen will depend on factors such as availability, cost, adverse effects, adherence and drug resistance. Future studies should assess these aspects. In addition, trials evaluating the long-term effects of anti-tuberculosis chemoprophylaxis, the optimal duration of TB preventive
therapy, the influence of level of immunocompromise on effectiveness and combination of anti-tuberculosis chemoprophylaxis with antiretroviral therapy are needed.

For full text access click here:
http://mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD000171/frame.html

Editors’ note: One-third of the world’s population has latent tuberculosis (TB) infection meaning that they are infected but have no symptoms. Once you are infected with TB, you are infected for life. The lifetime risk of progressing to active disease is about 10% but this soars to 30% or more in people with HIV infection who have a 5-10% annual risk of developing active TB. Several trials have shown that HIV-negative people who take isoniazid (INH) daily for 6 to 12 months have a substantially reduced risk of active TB. Daily INH also reduces the risk of active TB in people living with HIV, particularly those whose immune systems are healthy enough, as evidenced by a positive skin test to TB, to benefit from INH’s help. This updated Cochrane review confirms previous findings but calls for more research to find out how long people need to take preventive therapy and the best drug or drugs to take, either before or after antiretroviral treatment has started. Nonetheless, there is no justification to wait. All people with HIV should be assessed for TB, particularly in high TB prevalence settings, and if latently infected with TB they should placed on INH or combination anti-TB drugs. The challenge is to determine whether their TB infection is latent or active.

11. Men who have sex with men

Using Motivational Interviewing in HIV Field Outreach With Young African American.


Outlaw and colleagues sought to determine whether field outreach with motivational interviewing, as compared with traditional field outreach, leads to increases in HIV counselling and testing and rates of return for test results among young African American men who have sex with men. In a randomized, 2-group, repeated-measures design, 96 young African American men who have sex with men completed a motivational interviewing-based field outreach session and 92 young African American men who have sex with men completed a traditional field outreach session. The percentages of participants agreeing to traditional HIV counselling and testing (an oral swab of the cheek) and returning for test results were the primary outcome measures. More of the participants in the motivational interviewing condition than the control condition received HIV counseling and testing (49% versus 20%; chi²(1)=17.94; P=.000) and returned for test results (98% versus 72%; chi²(1)=10.22; P=.001). The addition of motivational interviewing to field outreach is effective in encouraging high-risk young African American men who have sex with men to learn their HIV status. Also, peer outreach workers can be effectively trained to reduce health disparities by providing evidence-based brief counselling approaches targeting high-risk minority populations.

For abstract access click here:

Editors’ note: Traditional field outreach entails a face-to-face interaction between an outreach worker and an individual in a natural environment, with a focus on delivering education and safer sex supplies. In this study, the outreach workers in the traditional group focused on risk assessment, provision of information in a nonjudgmental, respectful manner, and an offer of HIV testing and counselling. Only 20% of their clients chose to receive HIV testing and counselling compared to 49% of those who received the same field outreach as well as motivational interviewing. This consisted of assessment of readiness to learn HIV status, exploration of ambivalence about learning status with tailored education as needed, affirmation of specific strengths to boost self-confidence for behaviour change, and communication of respect for clients as the experts on their own behaviour, emphasising personal choice and responsibility. This is a
small study but the results are promising and in the end make common sense. Information is not enough to move many people to overcome their ambivalence to learning their HIV status and, for those who do make the step to have a test, to returning to learn their result. The additional peer outreach worker training, involving specific client-centred micro-skills and strategies to elicit and reinforce client motivations, generates the only added costs in this approach.

12. Comorbidities

Antiviral treatment for chronic hepatitis C in patients with human immunodeficiency virus.


Antiviral treatment for chronic hepatitis C may be less effective if patients are co-infected with human immunodeficiency virus (HIV). The aim of the review was to assess the benefits and harms of antiviral treatment for chronic hepatitis C in patients with HIV. Trials were identified through manual and electronic searches in The Cochrane Hepato-Biliary Group Controlled Trials Register, the Cochrane Central Register of Controlled Trials (CENTRAL) in The Cochrane Library, MEDLINE, EMBASE, and Science Citation Index Expanded. The last search was May 2009. Randomised trials comparing at least 12 weeks of any anti-HCV treatment versus another treatment regimen or no treatment were selected. Patients who had chronic hepatitis C and stable HIV irrespective of previous antiviral therapy were included. Data extraction and assessment of risk of bias were done in duplicate. Analysis was by intention-to-treat. Fourteen trials were included. None of the included 2269 patients were previously treated for chronic hepatitis C. Peginterferon (either 2a, 180 microgram, or 2b, 1.5 microgram/kg, once weekly) plus ribavirin was more effective in achieving end of treatment and sustained virological response compared with interferon plus ribavirin (5 trials, 1340 patients) or peginterferon (2 trials, 714 patients). The benefit of peginterferon plus ribavirin was seen irrespective of HCV genotype although patients with genotype 1 or 4 had lower response rates (27%) than patients with genotype 2 or 3 (56%). The remaining trials compared different treatment regimens in patients who were treatment naive or had no virological response after three months of treatment, but overall they had not enough power to show any effect of increasing the dose of interferon or adding both amantadine or ribavirin. The overall mortality was 23/2111 patients with no significant differences between treatment regimens. Treatment increased the risk of adverse events including anaemia and flu-like symptoms, and several serious adverse events occurred including fatal lactic acidosis, liver failure, and suicide due to depression. Peginterferon plus ribavirin may be considered a treatment for patients with chronic hepatitis C and stable HIV who have not received treatment for hepatitis C as the intervention may clear the blood of HCV RNA. Supporting evidence comes mainly from the analysis of this non-validated surrogate outcome assessed in comparisons against other antiviral treatments. There is no evidence on treatment of patients who have relapsed or did not respond to previous therapy. Careful monitoring of adverse events is warranted.

For full text access click here:
http://mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD004888/frame.html

Editors’ note: The prevalence of hepatitis C and HIV co-infection is highest among people who inject drugs and those who have received contaminated blood or blood products. After acute hepatitis C infection, only 5% of people with HIV infection spontaneously clear hepatitis C in comparison with 14 to 45% of people without HIV infection. Since the advent of effective three-drug antiretroviral treatment in 1996, end-stage liver disease due to hepatitis C has become the leading cause of death among patients with stable HIV. Patients responded poorly to available treatments for hepatitis C before the development of a pegylated form of interferon called ‘peginterferon’. Nonetheless, hepatitis C viral genotype, dose of treatment, and duration of therapy may affect the treatment response. This review found that more trials of combination treatment using peginterferon and ribavirin are needed to better determine the duration of treatment in HIV-infected patients who have hepatitis C genotype 2 or 3.

13. Impact
The effects of HIV/AIDS on rural communities in East Africa: a 20-year perspective.


Much of the research on implications of the HIV epidemic for individual households and broader rural economies in the 1980s and early 1990s predicted progressive declines in agricultural production, with dire consequences for rural livelihoods. Restudies in Tanzania and Uganda show that from 1986 to the present, HIV and AIDS have sometimes thrown households into disarray and poverty, but more often have reduced development. The progressive and systematic decline predicted in earlier work has not come to pass. However, poverty remains, as does endemic HIV disease.

For abstract access click here:

Editors’ note: South-western Uganda and north-western Tanzania had HIV prevalence levels approaching 30% of the population in the mid-1980s. Predominantly rural and dependent on agriculture, these communities experienced striking demographic impact in the 15 to 50 year age cohort. It was hypothesised that this household depletion would cause a progressive decline in the quantity and quality of agricultural production, increased numbers of orphans, and deepening poverty. These did not happen exactly as predicted because of the resilience of families and communities to the stress of HIV. Households employed a variety of coping strategies including replacement of lost household members, remittances from family members based on reciprocity, credit, and public assistance. When a household head died of AIDS, some households did dissolve and previous levels of agricultural production took up to a decade to be regained but many did reconstitute under a new household head. Fostering of children, already a common practice before the HIV epidemic, increased to 30-40% of households by 2007. But the impacts were most felt in the next generation, particularly for girl children who lost their mothers – they received less education and were shorter when they reached adulthood. The long-term development impacts of HIV in these areas of Uganda and Tanzania, though less dramatic than the household shocks of morbidity and mortality, are persistent poverty and deprivation, despite tremendous resilience, with the long wave effects of the HIV epidemic in these areas yet to be fully realised.

14. Basic Science

Cellular levels of HIV unspliced RNA from patients on combination antiretroviral therapy with undetectable plasma viremia predict the therapy outcome.


Combination antiretroviral therapy, the standard of care for HIV-1 infection, is considered to be successful when plasma viremia remains below the detection limit of commercial assays. Yet, combination antiretroviral therapy fails in a substantial proportion of patients after the apparent success. No laboratory markers are known that are predictive of combination antiretroviral therapy outcome in initial responders during the period of undetectable plasma viremia. Here, the authors report the results of a retrospective longitudinal study of twenty-six HIV-infected individuals who initially responded to cART by having plasma viremia suppressed to <50 copies/ml. Eleven of these patients remained virologically suppressed, whereas fifteen experienced subsequent combined antiretroviral therapy failure. Using sensitive methods based on seminested real-time PCR, they measured the levels of HIV-1 proviral (pr) DNA, unspliced (us) RNA, and multiply spliced RNA in the peripheral blood mononuclear cells (PBMC) of these patients at multiple time points during the period of undetectable plasma viremia on combination antiretroviral therapy. Median under-therapy level of usRNA was significantly higher (0.43 log(10) difference, P = 0.0015) in patients who experienced subsequent combination antiretroviral therapy failure than in successfully treated patients. In multivariate analysis, adjusted for baseline CD4(+) counts, prior antiretroviral therapy experience, and particular combination antiretroviral therapy regimens, the maximal usRNA level under therapy was the best independent predictor of
subsequent therapy failure (adjusted odds ratio [95% CI], 24.4 [1.5-389.5], P = 0.024). The only other factor significantly associated with combination antiretroviral therapy failure was prior antiretroviral therapy experience (adjusted odds ratio [95% CI], 12.3 [1.1-138.4], P = 0.042). Levels of usRNA under combination antiretroviral therapy inversely correlated with baseline CD4(+) counts (P = 0.0003), but did not correlate with either baseline usRNA levels or levels of prDNA under therapy. The authors conclude that their data demonstrate that the level of HIV-1 usRNA in PBMC, measured in combination antiretroviral therapy-treated patients with undetectable plasma viraemia, is a strong predictive marker for the outcome of therapy.

For full text access click here: http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0008490

Editors’ note: Ultrasensitive assays can detect low-level viraemia (virus in the blood) in people who have undetectable viral loads by standard commercial tests. It is unknown whether this reflects ongoing virus replication despite antiretroviral treatment or release of virus from stable reservoirs without new replication cycles. Likewise, whether the presence of intracellular virus reflects ongoing replication or viral production from stable reservoirs is unclear. This is the first study to find an association, and it was strong, between subsequent treatment failure and the level of unspliced RNA in peripheral blood mononuclear cells in people considered to be treatment successes with viral loads below 50 copies/ml. Furthermore, the unspliced RNA level was inversely associated with baseline CD4+ count, possibly explaining the link between baseline CD4+ count and risk of therapy failure. It is important that this study be replicated because it implies that testing the level of unspliced RNA may actually be a sensitive prognostic indicator, picking up drug-resistant escape mutants before treatment failure occurs.

15. Structural determinants

Effect of Economic Assets on Sexual Risk-Taking Intentions Among Orphaned Adolescents in Uganda.


The authors examined the effect of economic assets on sexual risk-taking intentions among school-going AIDS-orphaned adolescents in rural Uganda. AIDS-orphaned adolescents from 15 comparable schools were randomly assigned to control (n=133) or treatment (n=127) conditions. Treatment participants received child savings accounts, workshops, and mentorship. This economic intervention was in addition to the traditional care and support services for school-going orphaned adolescents (counselling and school supplies) provided to both treatment and control groups. Adolescents in the treatment condition were compared with adolescents in the control condition at baseline and at 10 months after the intervention. After control for sociodemographic factors, child caregiver/parental communication, and peer pressure, adolescents in the economic intervention group reported a significant reduction in sexual risk-taking intentions compared with adolescents in the control condition. The findings indicate that in Uganda, a country devastated by poverty and disease (including HIV), having access to economic assets plays an important role in influencing adolescents’ sexual risk-taking intentions. These findings have implications for the care and support of orphaned adolescents, especially in poor African countries devastated by poverty and sexually transmitted diseases.


Editors’ note: Two conceptual frameworks underpinned this trial which tested a combined microfinance youth empowerment and health promotion programme for adolescents orphaned by AIDS against health promotion alone. The first was risk and resilience theory which suggests that family resources, including economic assets, can buffer the effects of factors that would otherwise
push adolescents toward engaging in sexual risk behaviour. The second is asset theory, which posits that people with more present assets expect to have more in the future. By extension, adolescents who have an increased belief that their future holds the promise of success might reduce their risk of unsafe sex. This innovative trial found significantly lower intentions to engage in risky sex among the adolescents in the intervention arm which consisted of twelve 1 to 2 hour workshops on assets building and financial planning, a monthly mentorship programme with peer mentors on future planning, and a child savings account dedicated to paying for secondary schooling or a family small business, in addition to the health promotion received by the other group. The savings were matched 2 for 1 by the study and, in the end, all the subjects opted to use the funds for schooling rather than a small business. What may have happened is that participation in the programme instilled a sense of hope for the future that did encourage adolescents to be more careful in making decisions affecting their future. There is no doubt that further research addressing the multidimensional aspects of orphan hood, or for that matter of poverty among adolescents, is needed for a combination prevention approach that includes behavioural, biomedical, and structural components and that uses the incidence of HIV or sexually transmitted infections as endpoints.

That was HIV this week, signing off.
Editors’ notes on journal access

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