



Funding worries and threats to universal access dominate International Aids conference

In a matter of three days around 5,000 delegates, including scientific and medical experts on HIV/AIDS descended on Cape Town to attend the 5th International AIDS Society Conference on HIV Pathogenesis, Treatment and Prevention, but it was not business as usual.

What researchers, keen to share results of their latest studies – highlighting advances in basic and clinical science, biomedical prevention and operational research – found was not the normally placid scientific community eager to hear listen. They found a conference atmosphere dominated by the outrage over HIV/AIDS treatment funding cutbacks and dismay at international political will and commitment to keep promises of achieving universal access to antiretroviral treatment.

IAS president, Dr Julio Montaner, quoted in Canada's Globe and Mail, set the tone when he called the silence of G8 leaders on their broken promises to fight HIV/AIDS "criminal".

In 2005 at the Gleneagles summit world leaders pledged to strive for universal access to AIDS treatment by 2010, but their silence and grumblings over the global recession are seemed to suggest the political will was drying up fast – along with pledged funding for the AIDS fight.

"The silence of the G8 leaders is not just pathetic, it is criminal. We will not shut up on this issue...It will be a dominant issue this week [*at the conference*]. We will not be silent," Montaner said.

Before the opening of the conference MSF raised the alarm about the danger posed by possible ruptures, in the supply of critical AIDS drugs in six African counties, which would put thousands of patients' lives at risk.

Conference organisers picked up on MSF's concerns and invited Dr Eric Goemaere, MSF SA Medical Coordinator to take part in a special session where drug stock-outs and worries over funding were discussed.

"We need \$17 to 18 billion per year, or a total of \$123 billion over the next seven years, but all we have is \$20 billion, leaving us with a funding gap of \$103 billion," Goemaere told delegates. He added that the promises made to people living with HIV/AIDS during the seminal 2000 International AIDS Conference in Durban in 2000, that universal access to treatment was at hand, were being dashed. "We promised them treatment, and they came," Goemaere said. But now that promise was not renegeed and stalked by looming specter of a funding shortfalls.

MSF warned the stagnation of funding coupled with the high cost of new medicines meant that patients needing new drug regimens will return to AIDS death row. While the global need of seven million people to get access to AIDS drugs remains unaddressed, those patients being in developing countries and who are failing their first line treatment regimens, will have little hope of survival.

Data from MSF's public sector AIDS treatment partnership programme with Department of Health in Khayelitsha, indicated that 16 percent of patients experienced treatment failure on their first-line regimen within five years. And a quarter of those patients who were switched to a second-line regimen failed on this alternative treatment line within two years.

Because there is no third-line regimen available in South Africa, like in many other developing countries, these patients are now at risk of dying.

And if there is no urgent and focused push for change, what MSF has observed in Khayelitsha, is what will soon be seen throughout Africa, Goemaere warned.

Beyond the politically charged atmosphere, punctuated by protestors' cries for a drop in AIDS drug prices and uninterrupted funding, ([see the slideshow](#)) MSF had a significant presence at the conference, with over 30 abstracts accepted.

This included four oral presentations. MSF also organised 2 satellite meetings and participated in a number of others (Details of the various MSF inputs are available at <http://www.msf.org.za/2009-aids/>). The following provides an overview of presentations of interest to MSF programmes. All abstracts are available at <http://www.ias2009.org/pag/PosterExhibition.aspx>

TO KEEP YOU UP TO DATE WITH THE SCIENTIFIC HIGHLIGHTS OF THE IAS 2009 NATHAN FORD, HEAD OF MSF SA'S MEDICAL UNIT, PROVIDES THIS USEFUL SUMMARY.

For all those who were not able to attend the conference, consider this as your guide to getting an expert and clear view of the significance of the conference after the political dust has settled.

CLINICAL SCIENCE

HIV/TB

A pre-conference satellite addressed a number of issues relating to HIV/TB co-infection. Topics included:

Preventing TB in People Living with HIV: research priorities and way forward.

<http://www.ias2009.org/pag/PSession.aspx?s=2449#1>

TB in HIV-infected Children: addressing the research neglect.

<http://www.ias2009.org/pag/PSession.aspx?s=2449#2>

Drug resistance TB in People Living with HIV: research questions and priorities.

<http://www.ias2009.org/pag/PSession.aspx?s=2449#3>

Clinical challenges of diagnosing and treating TB in People Living with HIV: what next for research?

<http://www.ias2009.org/pag/PSession.aspx?s=2449#4>

When to start

Data from a randomized trial in Haiti (CIPRAHT001) provided strong evidence that early treatment initiation significantly improves survival. The study, which was stopped early, found a four-fold reduction in mortality and a two-fold reduction in incident TB among patients who started treatment earlier (CD4 350 cells/mm³) compared to those who started later (CD4 < 200 cells/mm³). In a plenary address former IAS president Pedro Cahn argued that the evidence for earlier initiation is overwhelming, and advocated abandoning d4T and introducing viral load monitoring in all programs to decrease the emergence of resistance.

http://www.ias2009.org/PAGMaterial/WEPL102_Cahn_1.ppt

Paediatrics

A randomized trial of switching to nevirapine-based therapy for infected children exposed to nevirapine prophylaxis (MOAB103) found that re-use of nevirapine following successful suppression on LPV/r-based therapy is possible under some circumstances for HIV-infected children exposed to nevirapine prophylaxis. Further research is necessary to determine the circumstances and interventions required to safely re-use this agent.

Infectious complications

A study from rural Uganda (TUPDB102) showed that septicaemia incidence was higher in HIV-infected than HIV-uninfected participants and only declined after the first year on ART, consistent with slow immune recovery. Determining the long-term impact of ART on HIV-related septicaemia requires longer follow-up. The most common microbiologic etiologies were *Streptococcus pneumoniae* and Non typhoid *Salmonella* which were 91% and 75% resistant to cotrimoxazole respectively.

HIV/HBV

An overview session (no abstract available) highlighted the fact that the mortality of HIV/HBV co-infected patients is significantly high: >14/100 patient-years, or one order of magnitude over that of either HBV or HIV alone. This is due to four main factors: virological factors (HbsAg titers do not significantly decline in HIV-infected individuals); immunological factors (there is reduced HBV-specific CD4+ T-cells in co-infected patients on HAART); hepatic factors (immune activation is an important pathophysiologic mechanism for HBV liver disease); and treatment factors (HAART hepatotoxicity compounding HBV-induced liver damage, and hepatic flare following discontinuation of HAART).

Lab monitoring

A sub-study of the DART trial looking at 5 year follow-up of creatinine and GFR in patients receiving and not receiving TDF first-line found that severe GFR was infrequent on all regimens and chronic kidney disease was only slightly more common in the TDF arm (TUPEB184). Another substudy of DART reported that cotrimoxazole prophylaxis reduced mortality by 50% in the first 72 weeks on ART, with no effect thereafter (MOPEB020). Finally, DART reported no benefit of 12 weekly CD4 monitoring on disease progression during first 2 years on ART (with targeted monitoring thereafter) (TUSS102). This is in contrast to a recent study published by several DART trialists which showed a clear benefit of viral load to identify early viral failures and limit the emergence of resistance (*Lancet Inf Diseases* 2009 9;7:409-17) and led to debate around the role of CD4 and viral load in resource-limited settings, with some suggestion of focusing only on viral load.

Antiretrovirals

A randomized trial comparing QD and BID dosing of LPV/r in HIV-1-infected antiretroviral-experienced subjects (TUAB104) found non-inferiority BID when co-administered with NRTIs in antiretroviral-experienced subjects, opening the way for once daily second-line regimens. Results from two drug trials held promise for treatment simplification in the developed world (and eventually the developing world if the price is right). Both the MONOI (abstract WELB102) and MONET (TUAB106-LB) trials reported non-inferior week 48 efficacy of darunavir/ritonavir monotherapy vs darunavir/ritonavir plus NRTIs. Switching to monotherapy would be expected to provide simpler dosing and reduce treatment costs.

BIOMEDICAL PREVENTION

New interventions

Results of all completed trials of STD control, microbicides, pre-exposure prophylaxis, HIV vaccines and male circumcision were summarized in a plenary address Ronald Gray (Johns Hopkins). Of 28 trials done to date only four have reported significant efficacy (all for male circumcision), leading to calls for fewer trials of better quality and a renewed emphasis on basic science, particularly for vaccine development.

http://www.ias2009.org/PAGMaterial/TUPL101_Gray_1.ppt

Treatment as prevention

A plenary by Reuben Granich (World Health Organization) summarized the potential role of antiretroviral treatment as a means of preventing transmission, following the publication of a model in

the Lancet last year suggesting a reduction in prevalence to below 1% by 2050 (Lancet 373;9657).
http://www.ias2009.org/PAGMaterial/MOPL101_Granich_1.ppt

Two presentations supported the role of increased antiretroviral coverage to prevent other infections: a study from Uganda (TUPDB104) showed that malaria incidence fell by 75% over a four-year period as HAART coverage increased, while a study from South Africa (WELBB105) found three-fold reduction in TB prevalence over a three year period among HIV-positive individuals.

HSV treatment as prevention

A trial (WELBC101) investigating the impact of herpes suppression with acyclovir on HIV transmission (3408 couples across 8 sub-Saharan African countries) found that the intervention did not reduce HIV transmission between partners (HR 0.92) but reduced genital ulcers by 73%.

PMTCT

Data from five studies supported the safety and efficacy of providing HAART to mothers during pregnancy and post-delivery to reduce vertical transmission. Among these, a randomized comparison of two triple-therapy combinations done in Botswana (WELBB101) found that vertical transmission reduced to 1% among breastfeeding mothers receiving HAART. Another study randomized 2367 mother-infant pairs randomized to one of the three antiretroviral viral intervention groups – infant extended nevirapine prophylaxis, maternal HAART, or ‘enhanced control’ (WELBC103). The primary endpoint was HIV transmission to the infant at 28 weeks, which was significantly reduced by both of the antiretroviral interventions, compared to control (infant NVP 1.8%, maternal HAART 3.0% vs. control 6.4%). Finally, a five-country trial (LBPEC01) that randomized pregnant women to triple therapy vs short-course prophylaxis (as recommended by WHO) found a 42% decrease in HIV transmission in the HAART group. These studies call for an urgent review of current WHO guidelines.

OPERATIONAL RESEARCH

Task shifting

A cluster-randomized trial of facility vs home-based care done jointly by researchers at the London School of Hygiene and Tropical Medicine and the Ugandan non-governmental organization TASO (MOAD101) found no difference in terms of mortality and virological suppression. Median annual patient costs for accessing care were five-times less via the home-based approach. Another important barrier to accessing care is the chronic shortage of doctors to provide antiretroviral therapy. To overcome this, nurse-based models of care have been proposed. Two studies – a randomized trial from South Africa (LBPED03) and a concordance study from Democratic Republic Congo (TUPED133) – found no difference in the performance of doctors and nurses in the provision of ART care, providing reassuring evidence of effectiveness. Finally, a study from Uganda reported reductions in patient waiting times due to task shifting (CDD091).

MSF models of care

Many of the contributions made by MSF were in the operational research track. Among these included: a costing study showing that in Thyolo, Malawi, the cost of providing universal access to ART was just \$2.5 per capita (TUAD105); a study from Chiradzulu, Malawi, showing greater survival and retention when ART is offered in decentralized compared to centralized sites (WEAD104); good outcomes after 5 years of providing ART in Cambodia (WEPED186 - 81% survival at 5 years) and South Africa (WEPED211 - 79.1% survival at 5 years, corrected for mortality among LTFU) with even higher success among children at 5 years in the same cohort (CDB109 - 98% survival at 5 years); successful provision of nurse-managed ART care in Lesotho (MOAD102); and clear advantages of HIV/TB integration, including a 7-fold increase in diagnosis of smear negative PTB (TUPED118).

BASIC SCIENCE

This track is of least interest to MSF practice but a couple of good plenaries summarized where the science is going. In a plenary session Dr Amalio Telenti (Institute of Medical Microbiology, Geneva) showed that 22% of population variance in viral load can explain population differences in viral load can be explained by common genetic variants, demographics and population factors. The use of such data may translate into helping clinicians predict of disease progression. Telenti also summarized evidence on the relationship between genetic determinants and plasma drug concentrations for a number of drugs that could provide guidance for dose-adjustment, potentially reducing cost and toxicity.

http://www.ias2009.org/PAGMaterial/MOPL102_Telenti_1.ppt

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July 2009*