



## HIV Care & PMTCT in Resource-Limited Settings

### Monthly Intelligence Report

### 2005, Vol 1, Issue 3

[Available on line](#)

#### prepared by the Bordeaux Working Group

**Members:** Elise Arrivé, Renaud Becquet, François Dabis (Coordinator), Valérie Leroy, Dominique Marchand, Evelyne Mouillet (Coordinator), Joanna, Orne-Gliemann, Freddy Perez, Charlotte Sakarovitch, Catherine Seyler, Besigin Tonwe-Gold.

**Number of citations selected for this issue: 24**

#### Subject headings / Subheadings indexing the selected references (by alphabetical order)

Adults / Women	Eastern Europe	Infant feeding / Breastfeeding	Prevention of Mother-To- Child Transmission (PMTCT) / AntiRetroViral (ARV)	Treatment impact and response
Children	Gynæcology	Infections (Others) / Prophylaxis	Prevention of sexual transmission	Treatment monitoring
Clinical manifestations (Others)	Hepatitis B infection (HBV)	Low Income Countries (LICs) / Africa, Asia, Caribbean, South America	Randomized Controlled Trial (RCT)	Treatment programme
Comprehensive care	Hepatitis C infection (HCV)	Mother-To-Child Transmission (MTCT)	Termination of pregnancy / Abortion	Tuberculosis (TB) / Prophylaxis
Conference summary	Highly Active AntiRetroviral Treatment (HAART)	Natural history	Treatment adherence	Viral resistance
Contraception	Industrialized countries	Obstetrics	Treatment complications	Voluntary Counselling and Testing (VCT)

**Citation format** (by alphabetical order of the authors): Author(s). **Title**. Source. **Abstr.** (Authors' abstract) or **Notes** (prepared by the Bordeaux Working Group) **Author address**, if available, **Subject Headings**

Bozzette SA. **Routine screening for HIV infection - Timely and cost-effective [Editorial]**. New England Journal of Medicine 2005;352(6):620-621.

**Introduction.** In the United States, HIV infection is generally discovered at an advanced stage, usually in the course of medical care and often during care for complications of AIDS. Earlier diagnosis would be far preferable, because it could speed access to appropriate care and increase the proportion of HIV-infected patients receiving care, thereby improving the quality of care for persons and populations. Two articles in this issue of the Journal indicate that widespread use of routine screening could offer these benefits and more at a reasonable cost. Paltiel and colleagues and Sanders and colleagues both predict that widespread use of routine screening will yield substantial benefits for HIV-infected patients. Paltiel et al estimate that the average CD4 count at the detection of HIV infection would rise from 154 to 210 cells per cubic millimeter and that the proportion of cases diagnosed at the time of an opportunistic complication would drop. These factors are important, because earlier access to antiretroviral therapy is likely to make it easier to suppress viral replication, improve immunity, and reduce drug-related adverse effects.<sup>4</sup> Consistent with this outcome, both studies estimate that the effects of screening would extend survival by 1.5 years for the average HIV-infected patient. These gains would come at a reasonable cost. The Centers for Disease Control and Prevention has recommended the routine use of screening in populations with a prevalence of HIV infection of 1 percent or greater. In such a population, Sanders et al and Paltiel et al estimate that the cost of one-time screening is \$41,736 and \$38,000 per quality-adjusted life-year gained, respectively; both estimates are less than the commonly cited threshold for cost-effective care of \$50,000 per quality-adjusted life-year gained. Cost-effectiveness changes with the prevalence of disease. Paltiel and colleagues estimate that in high-risk populations (those with a 3 percent prevalence of HIV infection), the costs would decrease to \$38,000 per quality-adjusted life-year gained, and in the general U.S. population (which has a 0.1 percent prevalence of HIV infection), the costs would increase to \$113,000 per quality-adjusted life-year gained. Repeated testing decreases efficiency, since it detects only incident cases. Given a 3 percent prevalence of HIV infection, Paltiel et al. estimate that testing every five years would cost \$50,000 per quality-adjusted life-year gained, and testing every three years would cost \$63,000 per quality-adjusted life-year gained. Overall, these results indicate that widespread use of HIV screening is consistent with commonly accepted standards for clinical practice when the prevalence of HIV infection is 1 percent or higher and that testing at five-year intervals may be a reasonable approach in some populations.

**Address:** Bozzette, SA; RAND Corp; Santa Monica, CA 90407; USA. [sbozzette@ucsd.edu](mailto:sbozzette@ucsd.edu)

**VCT**

De Baets AJ, Edidi BS, Kasali MJ, Beelaert G, Schrooten W, Litzroth A, Kolsteren P, Denolf D, Franssen K. **Pediatric human immunodeficiency virus screening in an African district hospital**. Clinical and Diagnostic Laboratory Immunology 2005;12(1):86-92.

**Abstr.** In order to evaluate alternative tests and strategies to simplify pediatric human immunodeficiency virus (HIV) screening at the district hospital level, a cross-sectional exploratory study was organized in the Democratic Republic of the Congo. Venous and capillary phlebotomies were performed on 941 Congolese children, aged 1 month to 12 years (153 children under 18 months and 788 children more than 18 months old). The HIV prevalence rate was 4.7%. An algorithm for children more than 18 months old, using serial rapid tests (Determine, InstantScreen, and Uni-Gold) performed on capillary blood stored in EDTA tubes, had a sensitivity of 100.0% (95% confidence interval [CI], 88.9 to 100.0%) and a specificity of 100.0% (95% CI, 99.5 to 100.0%). The results of this study suggest that the ultrasensitive p24 antigen assay may be performed on capillary plasma stored on filter paper (sensitivity and specificity, 100.0%; n = 87) instead of venous plasma (sensitivity, 92.3%; specificity, 100.0%; n = 150). The use of glucolets (instruments used to perform capillary phlebotomies), instead of syringes and needles, may reduce procedural pain and the risk of needle stick injuries at a comparable cost. Compared to the reference, HIV could have been correctly excluded based on one rapid test for at least 90% of these children. The results of this study point towards underutilized opportunities to simplify phlebotomy and pediatric HIV screening.

**Address:** De Baets, AJ; Inst Trop Med; Nutr & Child Hlth Unit; Nationalstr 155; B-2000 Antwerp; Belgium. [anisah2@attglobal.net](mailto:anisah2@attglobal.net)

**Children, LICs / Africa, VCT**

Harding R, Karus D, Easterbrook P, Raveis VH, Higginson IJ, Marconi K. **Does palliative care improve outcomes for patients with HIV/AIDS? A systematic review of the evidence**. Sexually Transmitted Infections 2005;81(1):5-14.

**Abstr.** Background: The need for palliative care in HIV management is underlined by the high prevalence of pain and symptoms, the toxicity, side effects, and virological failure associated with antiretroviral therapy, emergence of co-morbidities, continued high incidence of malignancies, late presentation of people with HIV disease, and the comparatively higher death rates among the infected individuals. Methods: A systematic review

was undertaken to appraise the effect of models of palliative care on patient outcomes. A detailed search strategy was devised and biomedical databases searched using specific terms relevant to models of palliative care. Data from papers that met the inclusion criteria were extracted into common tables, and evidence independently graded using well described hierarchy of evidence. Results: 34 services met the inclusion criteria. Of these, 22 had been evaluated, and the evidence was graded as follows: grade 1 (n = 1); grade 2 (n = 2); grade 3 (n = 7); grade 4 (n = 1); qualitative (n = 6). Services were grouped as: home based care (n = 15); home palliative care/hospice at home (n = 7); hospice inpatient (n = 4); hospital inpatient palliative care (n = 4); specialist AIDS inpatient unit (n = 2); and hospital inpatient and outpatient care (n = 2). The evidence largely demonstrated that home palliative care and inpatient hospice care significantly improved patient outcomes in the domains of pain and symptom control, anxiety, insight, and spiritual wellbeing. Conclusions: Although the appraisal of evidence found improvements across domains, the current body of evidence suffers from a lack of (quasi) experimental methods and standardised measures. The specialism of palliative care is responding to the clinical evidence that integration into earlier disease stages is necessary. Further studies are needed to both identify feasible methods and evaluate the apparent beneficial effect of palliative care on patient outcomes in the post-HAART era.

**Address:** Harding, R; Univ London Kings Coll; Guys Kings & St Thomass Sch Med; London SE5 9RS; England. [Richard.harding@kcl.ac.uk](mailto:Richard.harding@kcl.ac.uk)

**Adults, Comprehensive care, Industrialized countries**

Hogan DR, Salomon JA. **Prevention and treatment of human immunodeficiency virus/acquired immunodeficiency syndrome in resource-limited settings.** Bulletin of the World Health Organization 2005;83(2):135-143.

**Abstr.** Strategies for confronting the epidemic of human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) have included a range of different approaches that focus on prevention and treatment. However, debate persists over what levels of emphasis are appropriate for the different components of the global response. This paper presents an overview of this debate and briefly summarizes the evidence on a range of interventions designed to prevent the spread of HIV infection, paying particular attention to voluntary counselling and testing, treatment for sexually transmitted infections and prevention of mother-to-child transmission. We also review the experience with anti retro-viral-therapy to date in terms of response rates and survival rates, adherence, drug resistance, behavioural change and epidemiological impact. Although various studies have identified strategies with proven effectiveness in reducing the risks of HIV infection and AIDS mortality, considerable uncertainties remain. Successful integration of I treatment and prevention of HIV/AIDS will require a balanced approach and rigorous monitoring of the impact of programmes in terms of both individual and population outcomes.

**Address:** Salomon, JA, Harvard Univ, Sch Publ Hlth, Harvard Ctr Populat & Dev Studies, Cambridge, MA 02138 USA. [jsalomon@hsph.harvard.edu](mailto:jsalomon@hsph.harvard.edu)

**HAART, LICs, PMTCT, VCT**

Jeremy RJ, Kim S, Nozyce M, Nachman S, McIntosh K, Pelton SI, Yogev R, Wiznia A, Johnson GM, Krogstad P, Stanley K. **Neuropsychological functioning and viral load in stable antiretroviral therapy-experienced HIV-infected children.** Pediatrics 2005;115(2):380-387.

**Abstr.** Objective. Neuropsychological functioning and its correlation with viral load were investigated for previously treated HIV-infected children who underwent a change in treatment regimen. Methods. Thirteen age-appropriate measures of cognitive, neurologic, and behavioral functioning were administered to 489 HIV-infected children who were aged 4 months to 17 years and had been treated previously for at least 16 weeks with antiretroviral therapy. These clinically and immunologically stable children were randomized onto 1 of 7 drug treatment combinations, 6 of which included a protease inhibitor (PI), and evaluated prospectively for 48 weeks with respect to changes in neuropsychological performance and viral load. Results. Neuropsychological functioning was significantly poorer at baseline for the HIV-infected children as compared with established norms for their age. Children with higher viral load had poorer cognitive, both-hands fine-motor, and neurologic signs at baseline, but single-hand fine-motor and behavioral functioning were not correlated with viral load. After 48 weeks of treatment with PI-containing combination therapy, there was significant improvement in only the vocabulary score. Neuropsychological changes did not differ among the 6 PI-containing combination regimens. At week 48, even children with a viral load response below the level of detection (RNA<400 copies/mL) still showed poorer neuropsychological functioning compared with established norms. Conclusion. Poor neuropsychological functioning was seen for HIV-infected children and was worse for children with higher viral loads. Only 1 measure of neuropsychological functioning showed improvement after treatment with PI-containing combination therapy, and the extent of that improvement was relatively minor. Treatment strategies for children with HIV disease need to be reevaluated so that they consider restoration of neuropsychological functioning in addition to lowering the viral load.

**Address:** Jeremy, RJ; Univ Calif San Francisco; Sch Med; 505 Parnassus Ave; San Francisco; CA 94143; USA. [jeremyr@peds.ucsf.edu](mailto:jeremyr@peds.ucsf.edu)

**Children, Clinical manifestations (Others), Industrialized countries, HAART, Treatment impact and response**

Lucas MES, Deen JL, von Seidlein L, Wang XY, Ampuero J, Puri M, Ali M, Ansaruzzaman M, Amos J, Macuamule A, Cavailler P, Guerin PJ, Mahoudeau C, Kahozi Sangwa P, Chaignat C, Barreto A, Songane FF, Clemens JD. **Effectiveness of mass oral cholera vaccination in Beira, Mozambique.** *New England Journal of Medicine* 2005;352(8):757-767.

**Abstr.** BACKGROUND: New-generation, orally administered cholera vaccines offer the promise of improved control of cholera in sub-Saharan Africa. However, the high prevalence of human immunodeficiency virus (HIV) infection in many cholera-affected African populations has raised doubts about the level of protection possible with vaccination. We evaluated a mass immunization program with recombinant cholera-toxin B subunit, killed whole-cell (rBS-WC) oral cholera vaccine in Beira, Mozambique, a city where the seroprevalence of HIV is 20 to 30 percent. METHODS: From December 2003 to January 2004, we undertook mass immunization of nonpregnant persons at least two years of age, using a two-dose regimen of rBS-WC vaccine in Esturro, Beira (population 21,818). We then assessed vaccine protection in a case-control study during an outbreak of El Tor Ogawa cholera in Beira between January and May 2004. To estimate the level of vaccine protection, antecedent rates of vaccination were compared between persons with culture-confirmed cholera severe enough to have prompted them to seek treatment and age- and sex-matched neighborhood controls without treated diarrhea. RESULTS: We assessed the effectiveness of the vaccine in 43 persons with cholera and 172 controls. Receipt of one or more doses of rBS-WC vaccine was associated with 78 percent protection (95 percent confidence interval, 39 to 92 percent;  $P=0.004$ ). The vaccine was equally effective in children younger than five years of age and in older persons. A concurrently conducted case-control study designed to detect bias compared persons with treated, noncholeraic diarrhea and controls without diarrhea in the same population and found no protection associated with receipt of the rBS-WC vaccine. CONCLUSIONS: The rBS-WC vaccine was highly effective against clinically significant cholera in an urban sub-Saharan African population with a high prevalence of HIV infection.

**Address:** Deen, JL; Int Vaccine Inst; POB 14; Seoul 151600; South Korea. [jdeen@ivi.int](mailto:jdeen@ivi.int)

**Adults, Children, Infections (Others), LICs / Africa**

Malaba LC, Iliff PJ, Nathoo KJ, Marinda E, Moulton LH, Zijenah LS, Zvandasara P, Ward BJ, Humphrey JH. **Effect of postpartum maternal or neonatal vitamin A supplementation on infant mortality among infants born to HIV-negative mothers in Zimbabwe.** *American Journal of Clinical Nutrition* 2005;81(2):454-460.

**Abstr.** Background: Young infants are at risk of vitamin A deficiency. Supplementation of breastfeeding mothers improves the vitamin A status of their infants, but there are no data regarding its effect on infant mortality, and data on the effect of directly supplementing infants during the first few weeks of life are conflicting. Objective: The objective was to measure the effect on infant mortality of supplementing neonates and their HIV-negative mothers with single, large doses of vitamin A during the immediate postpartum period. Design: A randomized, placebo-controlled, 2-by-2 factorial design trial was conducted in 14 110 mothers and their infants; 9208 of the mothers were HIV-negative at delivery, remained such during the postpartum year, and were retained in the current analysis. The infants were randomly assigned within 96 h of delivery to 1 of 4 treatment groups: mothers and infants received vitamin A (Aa), mothers received vitamin A and infants received placebo (Ap), mothers received placebo and infants received vitamin A (Pa), and both mothers and infants received placebo (Pp). The vitamin A dose in the mothers was 400 000 IU and in the infants was 50 000 IU. The mother-infant pairs were followed to 12 mo. Results: Hazard ratios (95% CI) for 12 mo mortality among infants in the maternal-supplemented and infant-supplemented groups were 1.17 (0.87, 1.58) and 1.08 (0.80, 1.46), respectively. Hazard ratios (95% CI) for the Aa, Ap, and Pa groups compared with the Pp group were 1.28 (0.83, 1.98), 1.27 (0.82, 1.97), and 1.18 (0.76, 1.83), respectively. These data indicate no overall effect. Serum retinol concentrations among a subsample of women were similar to reference norms. Conclusion: Postpartum maternal or neonatal vitamin A supplementation may not reduce infant mortality in infants of HIV-negative women with an apparently adequate vitamin A status.

**Address:** Humphrey, JH; ZVITAMBO Project; 1 Borrowdale Rd; Harare; Zimbabwe. [jhumphrey@zvitambo.co.zw](mailto:jhumphrey@zvitambo.co.zw)

**Adults / Women, Children, LICs / Africa, Treatment impact and response**

Marston M, Zaba B, Salomon JA, Brahmbhatt H, Bagenda D. **Estimating the net effect of HIV on child mortality in African populations affected by generalized HIV epidemics.** Journal of Acquired Immune Deficiency Syndromes 2005;38(2):219-227.

**Abstr.** For a given prevalence, HIV has a relatively higher impact on child mortality when mortality from other causes is low. To project the effect of the epidemic on child mortality, it is necessary to estimate a realistic schedule of "net" age-specific mortality rates that would operate if HIV were the only cause of child death observable. We assume that this net pattern would be independent of mortality from other causes. We used African studies that measured the survival of HIV-infected children (direct data) or survival of children of HIV-infected mothers (indirect data). We developed a mathematic procedure to estimate the mortality of infected children from indirect data sources and obtained net HIV mortality patterns for each study population. The net age-specific HIV mortality pattern for infected children can be described by a double Weibull curve fitted to empiric data; this gives a functional representation of age-specific mortality rates that decline after infancy and rise in the preteens. The fitted curve that we would expect if HIV were the only effective cause of death shows 67% net survival at 1 year and 39% at 5 years. The curve also predicts 13% net survival at 10 years using constraints based on survival of infected adults.

**Address:** Marston, M; London Sch Hyg & Trop Med; Ctr Populat Studies; 49-51 Bedford Sq; London WC1B 3DP; England. [milly.marston@lshtm.ac.uk](mailto:milly.marston@lshtm.ac.uk)

**Children, LICs / Africa, Natural history**

Metcalf CA, Douglass JM, Malotte K, Cross H, Dillon BA, Paul SM, Padilla SM, Brookes LC, Lindsey CA, Byers RH, Peterman TA. **Relative efficacy of prevention counseling with rapid and standard HIV testing: A randomized, controlled trial - (RESPECT-2).** Sexually Transmitted Diseases 2005;32(2):130-138.

**Abstr.** Background: Two risk-reduction counseling sessions can prevent sexually transmitted diseases (STDs); however, return rates for test results are low. Study: A randomized, controlled trial compared rapid HIV testing and counseling in 1 visit with standard HIV testing and counseling in 2 visits. Main outcomes were STDs (gonorrhea, chlamydia, trichomoniasis, syphilis, HIV) within 12 months. Participants were 15- to 39-year-old STD clinic patients in Denver, Long Beach, and Newark. STD screening and questionnaires were administered every 3 months. Results: Counseling was completed by 1632 of 1648 (99.0%) of the rapid-test group and 1144 of 1649 (69.4%) of the standard-test group. By 12 months, STD was acquired by 19.1% of the rapid group and 17.1% of the standard group (relative risk [RR], 1.11; confidence interval [CI], 0.96-1.29). STD incidence was higher in the rapid-test group than in the standard-test group among men (RR, 1.34; CI, 1.06-1.70), men who had sex with men (RR, 1.86; 95% CI, 0.92-3.76), and persons with no STDs at enrollment (RR, 1.21; 95% CI, 0.99-1.48). Behavior was similar in both groups. Conclusions: Counseling with either test had similar effects on STD incidence. For some persons, counseling with standard testing may be more effective than counseling with rapid testing.

**Address:** Peterman, TA; Ctr Dis Control & Prevent; Mailstop E-02,1600 Clifton Rd NE; Atlanta, GA 30333; USA. [tpeterman@cdc.gov](mailto:tpeterman@cdc.gov)

**Industrialized countries, RCT, VCT**

Metcalf CA, Malotte CK, Douglass JM, Paul SM, Dillon BA, Cross H, Brookes LC, Dea Augustine N, Lindsey CA, Byers RH, Peterman TA. **Efficacy of a booster counseling session 6 months after HIV testing and counseling: A randomized, controlled trial - (RESPECT-2).** Sexually Transmitted Diseases 2005;32(2):123-129.

**Abstr.** Background: HIV counseling prevents sexually transmitted diseases (STDs), with most of the benefit accumulating in the first 6 months. Study: The authors conducted a multicenter, randomized, controlled trial of a 20-minute additional (booster) counseling session 6 months after HIV counseling compared with no additional counseling for prevention of STDs (gonorrhea, chlamydia, trichomoniasis). Participants were 15- to 39-year-old STD clinic patients in Denver, Long Beach, and Newark. Results: Booster counseling was completed by 1120 (67.8%) of 1653 assigned to receive it. An incident STD during the 6 to 12 months after initial counseling (and within the 6 months after scheduled booster counseling) was detected in 141 of 1653 (8.5%) participants in the booster counseling group and 144 of 1644 (8.8%) in the no-booster group (relative risk, 0.97; 95% confidence interval, 0.78-1.22). Three months after booster counseling, sexual risk behaviors were reported less frequently by the booster group than the no-booster group. Conclusions: Booster counseling 6 months after HIV testing and counseling reduced reported sexual risk behavior but did not prevent STDs.

**Address:** Peterman, TA; Ctr Dis Control & Prevent; Mailstop E-02,1600 Clifton Rd NE; Atlanta, GA 30333; USA. [tpeterman@cdc.gov](mailto:tpeterman@cdc.gov)

**Industrialized countries, RCT, VCT**

Monforte AD, Sabin CA, Phillips A, Sterne J, May M, Justice A, Dabis F, Grabar S, Ledergerber B, Gill J, Reiss P, Egger M. **The changing incidence of AIDS events in patients receiving highly active antiretroviral therapy.** Archives of Internal Medicine 2005;165(4):416-423.

**Abstr.** Background: Although the incidence of most AIDS events declines after initiation of highly active antiretroviral therapy (HAART), this decline is more rapid for some conditions than others. We herein describe the decline in incidence of AIDS-defining events among 12 574 antiretroviral-naive individuals who started HAART in the Antiretroviral Therapy Cohort Collaboration and determined whether the rate of decline is similar for events with different etiologies. Methods: Rates of AIDS were calculated for the periods 0 to 3, 4 to 6, 7 to 12, 13 to 24, and 25 to 36 months after starting HAART. Changes in incidence over time were investigated using Poisson regression. Results: During 22958 person-years of follow-up, 928 AIDS events developed (25.3% viral, 24.6% bacterial, 20.7% fungal, 8.1% protozoal, and 21.2% other). The incidence of any AIDS event declined from 129.3 (95% confidence interval [CI], 116.7-141.8) per 1000 person years in the first 3 months to 13.2 (95% CI, 9.4-17.0) in the third year after starting HAART (P<.001). The rate of decline in incidence was greatest for events with a viral etiology (87.0% per year) and lowest for those with a fungal etiology (54.0% per year). In the third year, fungal events represented 37.0% of AIDS events that occurred. After adjustment for the CD4 count and human immunodeficiency virus I RNA level, changes in the incidence of bacterial and viral events from months 0 to 6 and 7 to 12 remained significant, suggesting that changes in these markers did not fully explain the changes in incidence seen. Conclusion: Although the incidence of all AIDS-defining events decreased substantially after starting HAART, the pattern of decline was most pronounced for events with a viral etiology.

**Address:** Sabin, CA; Royal Free & Univ Coll; Sch Med; Royal Free Campus, Rowland Hill St; London NW3 2PF; England. [c.sabin@pcps.ucl.ac.uk](mailto:c.sabin@pcps.ucl.ac.uk)

**Adults, Clinical manifestations (Others), HAART, Industrialized countries**

Mseleku M, Smith TH, Guidozzi F. **HIV seropositive in pregnant South African women who initially refuse routine antenatal HIV screening.** Bjog an International Journal of Obstetrics and Gynaecology 2005;112(3):370-371.

**Abstr.** This study was instituted primarily to determine the HIV seroprevalence of pregnant South African women who refused routine HIV testing at the antenatal clinic of the Johannesburg Hospital, South Africa. Fifty such patients were identified, who, after being fully counselled and informed, agreed to participate in the study, provided total anonymity was adhered to: they did not want to know their results, irrespective of outcome. Blood specimens were given a laboratory reference number only, with no other reference to the patient and analysed utilising the ELISA immunoassay. Twenty-two of the 50 blood specimens, or 44% of patients analysed, tested positive for HIV. This is an alarming statistic, as the HIV prevalence in the general antenatal population at the Johannesburg Hospital is 29.4%.

**Address:** Guidozzi, F; Univ Witwatersrand; Johannesburg Hosp; 7 York Rd; ZA-2193 Johannesburg; South Africa.

**Adults / Women, LICs / Africa, VCT**

Nachega JB, Lehman DA, Hlatshwayo D, Mthopeng R, Chaisson RE, Karstaedt AS. **HIV/AIDS and antiretroviral treatment knowledge, attitudes, beliefs, and practices in HIV-infected adults in Soweto, South Africa.** Journal of Acquired Immune Deficiency Syndromes 2005;38(2):196-201.

**Abstr.** A cross-sectional study of knowledge, attitudes, beliefs, and practices (KABPs) toward HIV and antiretroviral therapy (ART) was conducted in Soweto, South Africa, using a standardized validated questionnaire. Of 105 HIV clinic patients evaluated, 70% of whom were not on ART, 89% had good knowledge about the cause of HIV infection and 83% knew about modes of transmission. Fifty-nine percent reported they were not worried about ART side effects. Sixty-five percent agreed that missing ART doses can lead to disease progression. Ninety percent had disclosed their HIV serostatus to 1 or more persons, but only 62% of those with a current sexual partner reported having told that partner. Approximately 80% reported that if they were taking ART, they would not be worried about family or friends finding out. Forty-nine percent believed that ART can cure HIV, a belief that was associated with a low level of education (P < 0.001). Overall, knowledge of the cause of HIV/AIDS, modes of transmission, and importance of ART adherence was good in our study population. Further research is warranted to assess the extent to which this knowledge and attendant attitudes predict ART adherence levels. The low rate of HIV serostatus disclosure to sexual partners calls for multidimensional interventions to reduce HIV-related stigma.

**Address:** Nachega, JB; Johns Hopkins Univ; Dept Int Hlth; 615 N Wolfe St, Room W5031; Baltimore; MD 21218; USA. [jnachega@jhsph.edu](mailto:jnachega@jhsph.edu)

**HAART, LICs / Africa, Treatment programme**

Paltiel AD, Weinstein MC, Kimmel AD, Seage GR, Losina E, Zhang H, Freedberg KA, Walensky RP. **Expanded screening for HIV in the United States - An analysis of cost-effectiveness.** New England Journal of Medicine 2005;352(6):586-595.

**Abstr.** BACKGROUND: Although the Centers for Disease Control and Prevention (CDC) recommend routine HIV counseling, testing, and referral (HIVCTR) in settings with at least a 1 percent prevalence of HIV, roughly 280,000 Americans are unaware of their human immunodeficiency virus (HIV) infection. The effect of expanded screening for HIV is unknown in the era of effective antiretroviral therapy. METHODS: We developed a computer simulation model of HIV screening and treatment to compare routine, voluntary HIVCTR with current practice in three target populations: "high-risk" (3.0 percent prevalence of undiagnosed HIV infection; 1.2 percent annual incidence); "CDC threshold" (1.0 percent and 0.12 percent, respectively); and "U.S. general" (0.1 percent and 0.01 percent). Input data were derived from clinical trials and observational cohorts. Outcomes included quality-adjusted survival, cost, and cost-effectiveness. RESULTS: In the high-risk population, the addition of one-time screening for HIV antibodies with an enzyme-linked immunosorbent assay (ELISA) to current practice was associated with earlier diagnosis of HIV (mean CD4 cell count at diagnosis, 210 vs. 154 per cubic millimeter). One-time screening also improved average survival time among HIV-infected patients (quality-adjusted survival, 220.7 months vs. 219.8 months). The incremental cost-effectiveness was \$36,000 per quality-adjusted life-year gained. Testing every five years cost \$50,000 per quality-adjusted life-year gained, and testing every three years cost \$63,000 per quality-adjusted life-year gained. In the CDC threshold population, the cost-effectiveness ratio for one-time screening with ELISA was \$38,000 per quality-adjusted life-year gained, whereas testing every five years cost \$71,000 per quality-adjusted life-year gained, and testing every three years cost \$85,000 per quality-adjusted life-year gained. In the U.S. general population, one-time screening cost \$113,000 per quality-adjusted life-year gained. CONCLUSIONS: In all but the lowest-risk populations, routine, voluntary screening for HIV once every three to five years is justified on both clinical and cost-effectiveness grounds. One-time screening in the general population may also be cost-effective.

**Address:** Paltiel, AD; Yale Univ; Sch Med; 60 Coll St; New Haven; CT 06520; USA. [david.paltiel@yale.edu](mailto:david.paltiel@yale.edu)

**Industrialized countries, VCT**

Regional Center for Quality of Health Care. **Handbook on Paediatric AIDS in Africa**, 2005.

**URL:** <http://www.rcqhc.org/modules.php?op=modload&name=UpDownload&file=index&req=getit&lid=49>

**Children, Comprehensive care, HAART, LICs / Africa, Natural history**

Rossi AD, Fonseca Carvasan GA, Makuch MY, Amaral E, Bahamondes L. **Factors associated with reproductive options in HIV-infected women.** Contraception 2005;71(1):45-50.

**Abstr.** A cross-sectional study was conducted in Campinas, Brazil, in HIV-infected women to evaluate factors associated with reproductive practices. A total of 112 HIV-infected women, 13 to 45 years old, with previous sexual experience were included in the study. Three groups were compared: pregnant women aware of their infection before current pregnancy, sterilized women who had made their reproductive choice after serodiagnosis and women using any reversible contraceptive method. Fisher's Exact Test and multivariate correspondence analysis were used in the statistical analysis. Among women interviewed, 23% were pregnant, 18% had been sterilized and 59% were using a reversible contraceptive method. Being younger was associated with reproductive practices that preserved the possibility of having a child. Reversible contraceptive users had fewer pregnancies and more often reported a desire to have children compared to the other groups. Partner's desire for parenthood was associated with pregnant and sterilized women. The clinical condition of the women and their partners, the serologic status of partner nor counseling about contraceptive choices influenced reproductive practices. (C) 2005 Elsevier Inc. All rights reserved.

**Address:** Amaral, E; UNICAMP; Dept Obstet & Gynecol; Caixa Postal 6181; BR-13084971 Campinas; SP; Brazil. [eliana@unicamp.br](mailto:eliana@unicamp.br)

**Adults / Women, Contraception, LICs / South Africa**

Sanders GD, Bayoumi AM, Sundaram V, Bilir SP, Neukermans CP, Rydzak CE, Douglass LR, Lazzeroni LC, Holodniy M, Owens DK. **Cost-effectiveness of screening for HIV in the era of highly active antiretroviral therapy.** New England Journal of Medicine 2005;352(6):570-585.

**Abstr.** BACKGROUND: The costs, benefits, and cost-effectiveness of screening for human immunodeficiency virus (HIV) in health care settings during the era of highly active antiretroviral therapy (HAART) have not been determined. METHODS: We developed a Markov model of costs, quality of life, and survival associated with an HIV-screening program as compared with current practice. In both strategies, symptomatic patients were identified through symptom-based case finding. Identified patients started treatment when their CD4 count dropped to 350 cells per cubic millimeter. Disease progression was defined on the basis of CD4 levels and viral load. The likelihood of sexual transmission was based on viral load, knowledge of HIV status, and efficacy of counseling. RESULTS: Given a 1 percent prevalence of unidentified HIV infection, screening increased life

expectancy by 5.48 days, or 4.70 quality-adjusted days, at an estimated cost of \$194 per screened patient, for a cost-effectiveness ratio of \$15,078 per quality-adjusted life-year. Screening cost less than \$50,000 per quality-adjusted life-year if the prevalence of unidentified HIV infection exceeded 0.05 percent. Excluding HIV transmission, the cost-effectiveness of screening was \$41,736 per quality-adjusted life-year. Screening every five years, as compared with a one-time screening program, cost \$57,138 per quality-adjusted life-year, but was more attractive in settings with a high incidence of infection. Our results were sensitive to the efficacy of behavior modification, the benefit of early identification and therapy, and the prevalence and incidence of HIV infection. **CONCLUSIONS:** The cost-effectiveness of routine HIV screening in health care settings, even in relatively low-prevalence populations, is similar to that of commonly accepted interventions, and such programs should be expanded.

**Address:** Sanders, GD; Duke Univ; Duke Clin Res Inst; POB 17969; Durham; NC 27715; USA. [gillian.sanders@duke.edu](mailto:gillian.sanders@duke.edu)

**Industrialized countries, VCT**

Semba RD, Ndugwa C, Perry RT, Clark TD, Jackson JB, Melikian G, Tielsch J, Mmiro F. **Effect of periodic vitamin A supplementation on mortality and morbidity of human immunodeficiency virus-infected children in Uganda: a controlled clinical trial.** *Nutrition* 2005;21(1):25-31.

**Abstr.** Objective: We investigated whether vitamin A supplementation would decrease mortality and morbidity rates in children infected with the human immunodeficiency virus (HIV). Methods: We conducted a randomized, double-blind, placebo-controlled clinical trial at Mulago Hospital, a large hospital that serves the urban and semiurban populations of Kampala, Uganda. One hundred eighty-one HIV-infected children were enrolled at 6 mo and randomized to receive vitamin A supplementation, 60 mg retinol equivalent, or placebo every 3 mo from ages 15 to 36 mo. Morbidity was assessed through a 7-d morbidity history every 3 mo, and vital events were measured. Children received daily trimethoprim-sulfamethoxazole prophylactic therapy. Results: After age 15 mo, children were followed for a median of 17.8 mo (interquartile range = 11.1 to 21.0 mo). The trial was stopped when there was a new policy to implement a program of mass supplementation of vitamin A in the country. Mortality rates among 87 children in the vitamin A group and 94 children in the control group were 20.6% and 32.9%, respectively, yielding a relative risk of 0.54 (95% confidence interval, 0.30 to 0.98;  $P = 0.044$ ) after adjusting for baseline weight-for-height Z score. Children who received vitamin A had lower modified point prevalences of persistent cough (odds ratio, 0.47; 95% confidence interval, 0.23 to 0.96;  $P = 0.038$ ) and chronic diarrhea (odds ratio, 0.48; 95% confidence interval, 0.19 to 1.18;  $P = 0.11$ ) and a shorter duration of ear discharge ( $P = 0.03$ ). Vitamin A supplementation had no significant effect on modified point prevalences of fever, ear discharge, bloody stools, or hospitalizations. Conclusions: Vitamin A supplementation decreases mortality rate in HIV-infected children and should be considered in the care for these children in developing countries. (C) 2005 Elsevier Inc. All rights reserved.

**Address:** Semba, RD; Johns Hopkins Univ; Sch Med; Baltimore; MD 21205; USA. [rdsemba@jhmi.edu](mailto:rdsemba@jhmi.edu)

**Children, LICs / Africa, Natural history, RCT, Treatment impact and response**

Teeraratkul A, Simonds RJ, AsavapiriyAnont S, Chalermchokcharoenkit A, Vanprapa N, Chotpitayasonondh T, Mock PA, Stat MA, Skunodum N, Neeyapun K, Jetsawang B, Culnane M, Tappero J. **Evaluating programs to prevent mother-to-child HIV transmission in two large Bangkok hospitals, 1999-2001.** *Journal of Acquired Immune Deficiency Syndromes* 2005;38(2):208-212.

**Abstr.** The 2 largest maternity hospitals in Bangkok implemented comprehensive programs to prevent mother-to-child HIV transmission in 1998. We conducted a cross-sectional survey of postpartum HIV-infected women in 1999 through 2001 to evaluate these programs. Women were given structured interviews at 0 to 3 days, 1 month, and 2 months postpartum. Medical records of women and their newborns were reviewed. Of 488 enrolled women, 443 (91%) had antenatal care: 391 (88%) at study hospitals and 52 (12%) elsewhere. The HIV diagnosis was first known before pregnancy for 61 (13%) women, during pregnancy for 357 (73%) women, during labor for 22 (5%) women, and shortly after delivery for 48 (10%) women. Antenatal zidovudine (ZDV) was used by 347 (71%) women, and intrapartum ZDV was used by 372 (76%) women. Twelve (55%) of the 22 women who first learned of their HIV infection during labor took intrapartum ZDV. All 495 newborn infants started prophylactic ZDV; the first dose was given within 12 hours for 491 (99%) children. Ten (2%) children were breast-fed at least once by their mother, and 10 (2%) were breast-fed at least once by someone else. Although uptake of services was high, inconsistent antenatal care, fear of stigmatization, and difficulty in disclosing HIV status prevented some women from using services.

**Address:** Teeraratkul, A; US Ctr Dis Control & Prevent Collaborat; TUC; DMS 6 Bldg, Tivanon Rd; Nonthaburi 11000; Thailand. [agt4@cdc.gov](mailto:agt4@cdc.gov)

**Adults / Women, Infant feeding / Breastfeeding, LICs / Asia, PMTCT / ARV, Treatment programme**

Van Rompay KKA, Abel K, Lawson JR, Singh RP, Schmidt KA, Evans T, Earl P, Harvey D, Franchini G, Tartaglia J, Montefiori D, Hattangadi S, Moss B, Marthas ML. **Attenuated poxvirus-based simian immunodeficiency virus (SIV) vaccines given in infancy partially protect infant and juvenile macaques against repeated oral challenge with virulent SIV.** *Journal of Acquired Immune Deficiency Syndromes* 2005;38(2):124-134.

**Abstr.** An infant macaque model was developed to test pediatric vaccine candidates aimed at reducing HIV transmission through breast-feeding. Infant macaques were given multiple immunizations during the first 3 weeks of life with recombinant poxvirus vaccines expressing simian immunodeficiency virus (SIV) structural proteins Gag, Pol, and Env (ALVAC-SIV or modified vaccinia virus Ankara [MVA]-SIV). After repeated daily oral inoculations with virulent SIVmac251 at 4 weeks of age, significantly fewer ALVAC-SIV-immunized infants were infected compared with unimmunized infants. Monkeys not infected after oral challenge in infancy were rechallenged at 16 months of age or older by repeated weekly oral SIV exposure; unimmunized animals were infected after fewer SIV exposures than were animals vaccinated with ALVAC-SIV or MVA-SIV. When infected, ALVAC-SIV- and MVA-SIV-vaccinated animals also had reduced viremia compared with unimmunized animals. The results of these investigations suggest that immunization of human infants with poxvirus-based HIV vaccine candidates may offer protection against early and late HIV infection through breastfeeding.

**Address:** Marthas, ML; Univ Calif Davis; Calif Natl Primate Res Ctr; Davis; CA 95616; USA.  
[mlmarthas@ucdavis.edu](mailto:mlmarthas@ucdavis.edu)

**PMTCT**

Villamor E, Misegades L, Fataki MR, Mbise RL, Fawzi WW. **Child mortality in relation to HIV infection, nutritional status, and socio-economic background.** *International Journal of Epidemiology* 2005;34(1):61-68.

**Abstr.** Background The aims of this study were to examine the impact of child HIV infection on mortality and to identify nutritional and sociodemographic factors that increase the risk of child mortality independent of human immunodeficiency virus (HIV) infection. Methods We conducted a prospective study in Dar es Salaam, Tanzania, among 687 children 6-60 months of age who were admitted to hospital with pneumonia. After discharge, children were followed up every 2 weeks during the first year and every 4 months thereafter. Sociodemographic characteristics were determined at baseline, and HIV status, haemoglobin, and malaria infection were assessed from a blood sample. During the first year of follow-up, we measured height, weight, and mid-upper arm circumference (MUAC) monthly. We estimated the risk of mortality according to HIV status and socio-economic characteristics using Cox proportional hazards models. Nutritional status variables (wasting and stunting) were examined as time-varying risk factors. Results Mean age at enrolment was 18 months. A total of 90 children died during an average 24.7 months of follow-up. HIV infection was associated with an adjusted 4-fold higher risk of mortality [relative risk (RR) = 3.92, 95% confidence interval (CI) 2.34-6.55, P < 0.0001]. Other risk factors included child's age <24 months, stunting, low MUAC, anaemia, and lack of water supply in the household. In models with time-varying covariates, stunting and wasting during the previous month were both significant and independently related to increased risk of death. HIV infection appeared to be a stronger predictor of mortality among children who were wasted than among those who were not (P for interaction = 0.05). Conclusions HIV infection is a strong predictor of death among children who have been hospitalized with pneumonia. Preventable conditions including inadequate water supply, child undernutrition, and anaemia contribute significantly to infant and child mortality independent of HIV infection.

**Address:** Villamor, E; Harvard Univ; Sch Publ Hlth; 665 Huntington Ave; Boston; MA 02115; USA.  
[evillamo@hsph.harvard.edu](mailto:evillamo@hsph.harvard.edu)

**Children, LICs / Africa, Natural history**

Wainberg MA. **Generic HIV drugs - Enlightened policy for global health [Editorial].** *New England Journal of Medicine* 2005;352(8):747-750.

**Introduction.** The 2000 International AIDS Conference in Durban, South Africa, focused the world's attention on disparities between rich and poor countries with respect to access to antiretroviral drugs. At that time, an estimated 7000 people in Africa had access to effective combination antiretroviral regimens. Though the number exceeds 100,000 today, it is still a far cry from the 8 million who are thought to require such therapy. In response, in 2003, the World Health Organization (WHO) launched an ambitious program termed "3 by 5" in an attempt to treat at least 3 million infected people by the end of 2005.

**Address:** Wainberg, MA; McGill Univ; Jewish Gen Hosp; Montreal; PQ H3T 1E2; Canada.  
[mark.wainberg@mcgill.ca](mailto:mark.wainberg@mcgill.ca)

**HAART**

Zhou J, Kumarasamy N, Ditangco R, Kamarulzaman A, Lee CKC, Li PCK, Paton NI, Phanuphak P, Pujari S, Vibhagool A, Wong WW, Zhang F, Chuah J, Frost KR, Cooper DA, Law MG. **The TREAT Asia HIV observational database - Baseline and retrospective data.** Journal of Acquired Immune Deficiency Syndromes 2005;38(2):174-179.

**Abstr.** Background: Relatively little is known regarding HIV disease natural history and response to antiretroviral treatments among Asian people infected with HIV. The Therapeutics Research, Education, and AIDS Training in Asia (TREAT Asia) HIV Observational Database (TAHOD) is a recently established collaborative observational cohort study that aims to assess HIV disease natural history in treated and untreated patients in the Asia-Pacific region. Methods: Observational data are collected on HIV-infected patients from 11 sites in the Asia-Pacific region. Data are centrally aggregated for analyses, with the first baseline and retrospective data transferred in September 2003. Retrospective data were analyzed to assess the response to highly active antiretroviral treatment (HAART) over a 6-month period in terms of changes in CD4 count and proportions of patients achieving an undetectable HIV viral load (<400 copies/mL). Results: By the end of May 2004, 1887 patients had been recruited to the TAHOD. Seventy-two percent of patients were male, with median age 36 years. Seventy-eight percent of patients reported HIV infection through heterosexual contact. Forty-three percent of patients had a previous AIDS diagnosis, of whom 55% had tuberculosis. The mean 6-month CD4 count increase was 115 cells/ $\mu$ L (SD = 127) after starting triple-combination therapy. Smaller CD4 count increases were associated with a higher CD4 count before starting treatment, prior treatment with monotherapy or double therapy, and treatment with a HAART regimen containing a nucleoside reverse transcriptase inhibitor (NRTI) and/or protease inhibitor (PI) but without a non-nucleoside reverse transcriptase inhibitor (NNRTI). Five hundred and ninety-eight patients started HAART and had a viral load assessment at 6 months, with 69% attaining an undetectable viral load. Older patients, patients not exposed to HIV through heterosexual contact, and patients treated with HAART containing NRTIs and NNRTIs but without PIs were found to be more likely to achieve an undetectable level. Conclusion: Analyses of retrospective data in the TAHOD suggest that the overall response to HAART in Asian populations is similar to that seen in Western countries.

**Address:** Zhou, J; Univ New S Wales; Natl Ctr HIV Epidemiol & Clin Res; Level 2,376 Victoria St; Darlinghurst; NSW 2010; Australia. [jzhou@nchecr.unsw.edu.au](mailto:jzhou@nchecr.unsw.edu.au)

**HAART, LICs / Asia, Natural history, Treatment impact and response, Treatment programme**

#### **CROI, Boston 22-25th February 2005.**

Conference reported by F Dabis, F Perez and B Towne-Gold. See CROI website for selected presentations quoted: \*, <http://www.retroconference.org/2005/Pages/webcasts.htm>

#### **Impact of Antiretroviral Therapy during Pregnancy**

**Palombi** et al (Abstract 67) presented results regarding the safety and effectiveness of HAART in a cohort of 778 women treated with triple ARV drugs combinations during pregnancy in Mozambique and found 6% grade 3-4 hepatotoxicity, 3% skin rash incidence and an HIV transmission rate at 1 and 6 months of age of 4.1 and 6.1 respectively. The authors also found low rates of mutations associated with drug-resistance (3 /20 samples tested).

Another abstract (**Machado** et al, Abstract 808) looking at pregnancy outcomes in women receiving HAART prior to conception showed that HIV-infected pregnant women had a higher risk of emergency caesarean section and of delivering a baby of low birth weight, but however preterm delivery, congenital anomalies, and complications in the newborn did not seem to be increased in this situation.

**Thomas** et al (Abstract 809) found rates of 8% of serious hepatic or cutaneous adverse events among pregnant women (n=241) on NVP-containing HAART regimens in Kisumu, Kenya. The authors found similar rates to other trials with non pregnant individuals receiving NVP-containing HAART and did not report an increased risk for women with CD4 counts > 250 cells/mm<sup>3</sup>. Similarly, **Phanuphak** et al (Abstract 21) presented results from Thailand regarding severe adverse events in 342 pregnant women on HAART. The authors found 9.4% grade III-IV liver toxicities and/or skin toxicities in pregnant women but no difference with non pregnant populations. A slight trend of higher rates was found with CD4 > 250 cells/mm<sup>3</sup>, but none reached statistically significant levels.

#### **Pregnancy and PMTCT**

**Kuhn** et al (Abstract 70) found no increase in maternal mortality attributable to prolonged breastfeeding among HIV+ women as part of a randomized trial (Lusaka Zambia). In a late breaker presentation, **Dabis**\* et al (Abstract 72LB) in the ANRS Ditrane Plus Study in Adijan, Côte d'Ivoire found that addition of 3 days of ZDV+3TC postpartum to a short course of ZDV+ 3TC and single dose NVP (SD-NVP) provides low rates of NVP resistance mutations and high efficacy in preventing peripartum HIV 1 transmission. The authors found a 6-week HIV-1 transmission rate of 4.7% (95%CI 2.4 to 7.0%) and the overall frequency of resistance mutations was 1.14% (CI 0.03 to 6.17%) for NVP and 8.33% (CI 3.66 to 15.76%) for 3TC.

**Duarte** et al (Abstract 69) in the NICHD Perinatal Study tested the hypothesis of a higher risk of post partum morbidity (PPM) with elective C section (ECS) than with vaginal delivery among HIV-1-infected women in Latin America and the Caribbean. Overall, they found that there was no statistically significant association between mode of delivery and major postpartum morbidity (vaginal [2.1%]; ECS [2.2%]; NECS [6.7%] ;  $p = 0.07$ ). but women with NECS were almost 10 times more likely to have minor postpartum morbidity than those who delivered vaginally ( $p = 0.03$ , OR = 9.6).

**Gonzalez-Tome** et al (Abstract 68) presented their results on the prevalence of gestational diabetes in pregnant women on ART. The prevalence rate was 7 % (CI 95%: 5.2 to 9.5) which is higher than in the general population. Only older age (OR 1.9, CI: 1 to 1.18) and protease inhibitor exposure (OR 2.3, CI: 1 to 5.3) remained as independent risk factors in this Spanish study

**Shapiro** et al (Abstract 74LB) presented the results of the MASHI trial in Botswana to prevent perinatal and breastfeeding MTCT in which all women received ZDV from 34 weeks gestation through delivery, and all infants received 1 month of ZDV. Mother-infant pairs were randomized to receive blinded maternal and infant SD-NVP (N/N) or maternal and infant placebo (P/P), and randomized to formula feed or breastfeed with 6 months of infant ZDV prophylaxis. In response to the publication of external data, the perinatal NVP intervention was modified and the revised study aim was to assess equivalence of P/N to N/N. In conclusion, this study found that adding N/N to ZDV was not superior to ZDV alone, but the authors stressed the need for these results to be interpreted cautiously in the context of feeding strategy and the in utero infection rate. Following this first presentation, **Thior** et al (Abstract 75 LB) compared the two different types of feeding interventions (FF vs BF plus ZDV) to prevent postnatal transmission in the same study sample. The primary efficacy endpoints for the feeding interventions were 7-month HIV positivity and 18-month HIV-free survival. The authors found that the BF+ZDV arm had higher HIV infection and lower mortality rates than the FF arm by 7 months and comparable HIV-free survival rates by 18 months.

Vertical transmission and antiretroviral resistance

**Johnson** et al (Abstract 100) in their study using the most sensitive resistance assays to better detect the emergence of resistance following SD-NVP, found the presence of K103N in an additional 40% of women with previously undetectable resistance, suggesting that only a minority of women receiving SD-NVP do not develop resistance mutations, and that conventional sequencing substantially underestimates the emergence of resistance. However in a late breaker abstract (73 LB), Westreich et al described the use of a stochastic model to predict the impact of NVP resistance on long term survival. Simulations of 20 years of follow-up in cohorts of 10,000 pregnant sub-Saharan African women were used and 4 scenarios were considered ;( SD-NVP PMTCT with 100, 50, and 10% subsequent access to HAART in eligible women). They were compared to HAART-based PMTCT (HAART during pregnancy and 6 months' lactation) with 100% subsequent HAART access. Assumptions made were that SD-NVP doubled risks of both initial failure of HAART and longer term virologic failure for those initially suppressed. This model predicted that with 100% access to HAART, the effect of NVP resistance on long-term survival is small and suggests that the effect of NVP resistance on mortality may not be apparent for many years; and, once it appears, may be small and that current forecasts may exaggerate the influence of NVP resistance on survival. The authors conclude that concerns about NVP resistance should not slow roll-out of non-HAART PMTCT, and that wide access to HAART will have vast public health benefits in the developing world.

In a plenary session (Abstract 8), **James McIntyre\*** spoke about the controversies surrounding SD-NVP for the PMTCT. He pointed out the fact that although SD-NVP has provided the impetus to extend PMTCT programmes in a number of countries, it has also attracted a great deal of controversy, including allegations that it is a “western conspiracy” or a “second rate strategy” for poor countries, that the studies have been unethical or inadequate, that the drug is extremely toxic or that high rates of resistance will result. However the author stated quite clearly that the only major disadvantage of the regimen is the risk of selection of NVP-resistant virus, and the potential impact on future pregnancies and on future treatment options. Detectable levels of NNRTI resistant virus are found six weeks post partum after SD-NVP in 20 – 50% of mothers and in around half of the HIV-infected infants. The longer term implications of this are not fully understood, but remain concerning. Preliminary data from a study by McIntyre group using a short postpartum course of zidovudine and lamivudine (4 or 7 days) to reduce the selection of resistance have shown a noticeable reduction in detectable resistance to around 10%. The author stressed that current PMTCT programmes still only reach 5% of all HIV-infected pregnant women and it is therefore important that antiretroviral regimens remain simple and feasible, while protecting the health of both mothers and children.

**Giuliano** et al (Abstract 99) presented the results of the evaluation of resistance mutations in the SIMBA trial (ZDV+ DDI from 36 weeks gestation until 1 week post-partum when they were randomized to receive daily lamivudine or NVP for the duration of breastfeeding or until HIV infection was confirmed) The authors concluded that post-partum long term prophylaxis with NVP or lamivudine leads almost invariably to the selection of resistance mutations in infected children and this should be taken into account when putting children on treatment.

**Gray et al** (Abstract 19) showed in their Uganda study that pregnancy represents a special period of increased risk of HIV acquisition, and therefore stressed that there is an urgent need to promote HIV prevention during pregnancy.

### **Scaling up HIV care in the developing world (special session)**

**El-Sadr\*** et al (Abstract 1) spoke about models of care. The need to provide care and treatment in a comprehensive context was described, the disparities that exist in the world with regard to antiretroviral drug access was highlighted. Models of HIV care need to consider: disease stage-specific interventions as well as local circumstances, i.e. the geographical setting and availability of services.

**Mermin\*** et al (Abstract 2) stated the importance of dealing with families on a comprehensive basis with regard to both HIV prevention and therapy. The need to scale up the production of appropriate antiretrovirals and make them available to people in Africa on an expeditious basis was highlighted. This would need to be done together with training programmes for health staff. In addition, low-cost measures to prevent death among HIV-infected persons in Africa need to be implemented on a large scale, including prophylactic use of trimethoprim/sulfamethoxazole (cotrimoxazole), isoniazid (INH) prophylaxis for tuberculosis, home-based water purification devices, and mosquito nets to prevent transmission of malaria.

**Martin\*** et al (Abstract 3) indicated that laboratory infrastructure is an important component of the scaling up of antiretroviral therapy options in all HIV-affected and endemic countries for various reasons: 1) to ensure that monitoring of CD4+ cell counts can occur in a manner that is quality-assured as well as economically viable; 2) to assess patient viral loads and the monitoring of individuals to assess responsiveness to therapy and ; 3) to test for antiviral resistance as a guide to choose antiretroviral drugs.

**Kim\*** et al (Abstract 6) spoke on behalf of WHO of the need to intervene now with antiretroviral drugs to prevent more deaths and hardship than has already occurred and presented the "3-by-5." strategy and its achievements till date: 700 00 patients on ART which represents 12% of the 5.8 million people in need of treatment in developing and transitional countries.

**Morpeth et al** (Abstract 638a) reported on the evaluation of clinical staging and simple low-cost laboratory tests as surrogates for CD4 count  $< 200 \times 10^6/L$  ( $<200$ ) to guide treatment decisions for starting antiretroviral therapy (ART) in resource-limited settings. Factors associated with CD4  $< 200$  were total lymphocyte count  $< 1.2 \times 10^9/L$  (odds ratio [OR] 14.8,  $p < 0.001$ ), erythrocyte sedimentation rate  $> 80\text{mm}/\text{hour}$  (OR 5.2,  $p < 0.001$ , se 74%, sp 66%), low hemoglobin concentration ( $< 11.4\text{g}/\text{dL}$  women,  $< 13.1\text{g}/\text{dL}$  men) (OR 4.7,  $p = 0.002$ , se 74%, sp 63%), total white blood cell count  $< 3.5 \times 10^9/L$  (OR 7.9,  $p=0.004$ , se 29%, sp 95%) and low hematocrit ( $< 35\%$  women,  $< 38\%$  men) (OR 3.3,  $p = 0.027$ , se 82%, sp 41%), BMI  $< 18\text{kg}/\text{m}^2$  (OR 3.4,  $p = 0.035$ , se 32%, sp 88%), bed-ridden at all (OR 8.4,  $p = 0.025$ , se 18%, sp 98%) and papular pruritic eruption (OR 3.1,  $p = 0.038$ , se 35%, sp 85%). WHO clinical stage and other specific staging conditions were not associated with CD4  $< 200$ . The authors concluded that clinical history, examination findings, anthropometry, and simple low-cost hematology tests can be used to identify patients with CD4  $< 200$  in developing countries.

**Stringer et al** (Abstract 638b) reported the feasibility of scaling-up ART services in Zambia based on a programme which includes training, renovation of clinical and laboratory facilities, a monitoring system and provision of clinical care. First-line drug regimens were zidovudine (ZDV) or stavudine (d4T) + lamivudine (3TC) + nevirapine (NVP). During the first six-month period, 9 740 patients were enrolled into HIV care and 6 054 started ART based on CD4 or clinical eligibility. Over 5132 patient-months of follow-up (1 043 patients), 110 patients died (crude death rate 0.021 death / patient-month); 42% of deaths occurred in patients whose entry CD4  $\leq 50$ , and 71% died within 60 days of enrolment. In multivariable logistic regression, ART appeared protective against death (RR = 0.7; 95%CI 0.3 to 1.4) after adjustments were made for CD4 and WHO stage. Risk of death remained strongly associated with WHO stage, body mass index  $< 16$ , and hemoglobin  $< 8$ .

### **Prevention, diagnosis and treatment of HIV in developing countries**

**Mutuluzza et al** (Abstract 22) showed results from the DART trial in which naïve patients received fixed dose ZDV/3TC and Tenofovir as initial treatment and found good virological response at 24 weeks comparable to responses in populations with low CD4 ( 50% were  $<100\text{CD}4$ ) with PI and NNRTI based regimens. This result is encouraging in the light of earlier data suggesting suboptimal viral potency with 3 NRTIs regimen and the advantage of such regimens apart from preserving the other two classes for second line are the possible concomitant use with rifampicine and possible use during pregnancy. Also Rey et al (Abstract 599) found an early successful virological response using ZDV/3TC and Tenofovir and described this combination as a viable triple NRTI regimen in treatment naïve patients. In the DART trial again, Ssali et al (Abstract 24) described an high incidence of anaemia with 6.6% episodes of grade 4 anaemia at a median of 12 weeks on HAART. This prevalence is probably increased by poor nutrition, malaria and other contributing factors. The authors stress the fact ART related anaemia is easily detectable and reversible and it is important to educate patients and HCWs.

**Kumarasany et al** (Abstract 583) showed the interim analysis of an STI trial (1 week off and 1 week on) in 30 patients who had successfully completed the 6 months period after randomisation. The authors found that the

STI arm was successful in maintaining CD4 above 200 and suppressing VL (87% in continuous HAART arm versus 80% in STI arm had < 400 copies/ml)

**Dabis** et al (Abstract 23) presented data on immune and viral responses from 3 048 HIV patients in 12 low-income countries (ART-LINC Cohort Collaboration). This data was compared with data available from developed countries (ART Cohort Collaboration [ART-CC]). The median number of CD4+ cells gained from baseline to six months was similar between the two groups (92 in ART-LINC vs 90 in ART-CC). In addition, the proportion of patients with undetectable viremia at six months was 71.4% in the developing world and 72.2% in the developed world. Despite similar responses to treatments, patients in the ART-LINC study were more likely to die. Mortality after one year was 5.8% for ART-LINC compared with 1.6% for the ART-CC group. The higher mortality rate was probably due to the high rate of opportunistic infections in low-income countries. 94% of the HAART patients in low-income countries are alive after one year of treatment. The most interesting factor associated with better survival in multivariate analysis in this context was the fact that patients had access to free care.

**Toro** et al (Abstract 621) assessed the response to ART in patients enrolled in the MTCT+ initiative, ongoing in eight countries in Sub-Saharan Africa and Thailand. Baseline demographic information, weight, and CD4+ cell count were assessed. MTCT-Plus enrolled 3352 adults as of July 2004. ARV was prescribed to 1017 (30.3%) pts of whom 226 were eligible for analysis (6 months of continuous ARV). Characteristics of the cohort: mean age 31 years, World Health Organization (WHO) stage at baseline I = 88 (39%), II = 62 (27.4%), III = 64 (28.3%), IV = 12 (5.3%), median CD4+ count 150 cells/mm<sup>3</sup> (IQR 85 to 192) [women baseline CD4+ count 150 cells/mm<sup>3</sup> (IQR 91-193), men baseline CD4+ cell count 147 cells/mm<sup>3</sup> (IQR 85 to 189)], and mean weight 59kg (IQR 52 to 64). At 6 months follow up (n = 226), median CD4+ count increased to 265 cells/mm<sup>3</sup> (IQR 187 to 360) (p < 0.0001) and weight (n = 145) to 61 kg (IQR 54 to 67kg) (p < 0.0001). Mean change in CD4 cell count in women was 148 cells/mm<sup>3</sup> and in men 107 cell/mm<sup>3</sup> (p < 0.006). The authors concluded that patient enrolled from multiple sites in resource-limited countries had favourable response to ARV.

The declining prevalence of HIV infection in Uganda has been attributed to increased rates of abstinence and monogamy. Wawer et al (Abstract 27LB) evaluated the impact of the "ABC" (abstinence, be faithful, use condoms) program on mortality over the last decade. HIV-related deaths (D) and viral epidemiology/early infection (E) were added to the analysis. 44 communities were followed over a ten-year period including data for 10,000 adults. A significant decline in HIV prevalence over the last decade was reported. Overall, age-standardized HIV prevalence declined significantly in all adults, from 17.6% to 11.4% (p = 0.007) and in young adults, from 16.9% to 7.7%, but no significant changes were noted in adolescents. Mortality was cited as the single factor that appears to have the greatest impact on the downward trend in prevalence. No increase in abstinence or monogamy was observed. A significant increase in condom use among adults and adolescents and among both males and females, particularly in casual relationships, was reported. The overall HIV incidence in young adults and adolescents remained relatively stable. This data suggests that the decline is primarily the result of increased condom use and HIV-related deaths.

### **Paediatric issues in developing countries**

**Puthanakit** et al (Abstract 54) reported on results of the study looking at the effectiveness of nevirapine (NVP)- and efavirenz (EFV)-based HAART in advanced-stage, ART-naïve children participating in the Thai national access program. 96 HIV-infected ART-naïve children, whose CD4 cells ≤ 15% were enrolled over a 10-month period and followed for >72 weeks. NVP-based HAART consisted of a generic non-paediatric fixed-dose combination of stavudine (d4T), lamivudine (3TC), and NVP (n = 51). EFV-based HAART utilized non-paediatric pills of d4T, 3TC, and EFV (n = 45). The drug dosage was calculated based upon the child's body weight. Adherence rate of ≥ 95% of prescribed dose at every visit was reported in 86% of patients. In an intention-to-treat analysis, plasma viral load was undetectable in 74% of patients (NVP 59%, EFV 91%; p < 0.001). At week 72, the median percentage of CD4 was 21 % (IQR 15 to 25). Children with virologic success had a significantly higher percentage of CD4 at week 72 (21% vs 15%, p = 0.02). The mean adjusted weight and height z-scores significantly improved to -1.4 (SD 0.9) and -2.1 (SD 1.3), respectively; 14 patients (NVP 12, EFV 2) developed resistance mutation virus. The authors concluded that NNRTI-based HAART is an effective regimen for HIV-infected children despite initiation of treatment in the advanced stage of disease and that the use of generic fixed-dose formulations and non-paediatric formulations are feasible and effective in resource-limited settings.

As part of the symposium on clinical paediatric issues in developing countries, two presentations were of particular interest. **Humphrey** et al (Abstract 106) reported on the results of the Zimbabwean study looking at the role of infant feeding practices on postnatal transmission (PNT). As part of a RCT evaluating postpartum vitamin A supplementation study, 4495 mothers were identified as HIV-positive; 2060 of their infants were PCR-negative at 6 wk and provided complete feeding data to 3 mo. All initiated breastfeeding; 156 (7.6%), 490 (23.8%), and 1414 (68.6%) infants were exclusively breastfed (EBF: only breast milk), predominantly (PBF) (breast milk + non-milk liquids), or mixed breastfed (MBF), respectively, during the first 3 months of life.

Compared with EBF, MBF was associated with 4.03 (CI 95%: 0.98, 16.61), 3.79 (CI: 1.40-10.29), and 2.60 (CI: 1.21-5.55) greater risks of PNT at 6, 12, and 18 months, respectively. PBF was associated with a 1.6 – 2.6 greater risk. Mothers exposed to the program were 70% more likely to learn their HIV status early (< 3 mo) and 8.4 times more likely to EBF. Each additional program contact was associated with a significant reduction in PNT. Early confirmation of pediatric HIV infection is essential to be in a position to initiate ARV treatment. **Rouzioux** et al (Abstract 107) reported on results of a new low cost molecular technique based on real time PCR for resource-limited settings. Results show that after a two-year large-scale use of this new technology in the field in several African and South East countries, HIV diagnosis in children is simple and reliable in comparison to commercial kits, and at least as feasible, even under difficult circumstances. One of the main concerns is still the feasibility of molecular techniques in laboratories with restricted conditions.

#### **Conference summary**