HIV Care & PMTCT in Resource-Limited Settings

Monthly Intelligence Report

Back Issues on Line

prepared by the Bordeaux Working Group

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Citation format (by alphabetical order of the authors): Author(s). Title. Source. Abstr. (Authors' text) or Introduction (Authors' text) or Selection (Selected sections of the paper) or Notes or Abstr. Edited (Written by the Bordeaux Working Group). Author Address, if available, Free Full Text, if available.
Abstr. Objectives: We report on a nonrandomized intervention cohort study to increase exclusive breast-feeding rates for 6 months after delivery in HIV-positive and HIV-negative women in KwaZulu-Natal, South Africa. Methods: Lay counselors visited women to support exclusive breast-feeding: four times antenatally, four times in the first 2 weeks postpartum and then fortnightly to 6 months. Daily feeding practices were collected at weekly intervals by separate field workers. Cumulative exclusive breast-feeding rates from birth were assessed by Kaplan-Meier analysis and association with maternal and infant variables was quantified in a Cox regression analysis. Findings: One thousand, two hundred and nineteen infants of HIV-negative and 1217 infants of HIV-positive women were followed postnatally. Median duration of exclusive breast-feeding was 177 (R=1-180; interquartile range: 150-180) and 175 days (R=1-180; interquartile range: 137-180) in HIV-negative and HIV-positive women, respectively. Using 24-h recall, exclusive breast-feeding rates at 3 and 5 months were 83.1 and 76.5%, respectively, in HIV-negative and HIV-positive women. Using the most stringent cumulative data, 45% of HIV-negative and 40% of HIV-positive women adhered to exclusive breast-feeding for 6 months. Counseling visits were strongly associated with adherence to cumulative exclusive breast-feeding at 4 months, those who had received the scheduled number of visits were more than twice as likely to still be exclusively breast-feeding than those who had not (HIV-negative women: adjusted odds ratio: 2.07, 95% confidence interval: 1.56-2.74, P < 0.0001; HIV-positive women: adjusted odds ratio: 2.86, 95% CI 2.13-3.83, P < 0.0001). Conclusion: It is feasible to promote and sustain exclusive breast-feeding for 6 months in both HIV-positive and HIV-negative women, with home support from well trained lay counselors.

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Abstr. Background: The World Health Organization recommends a single-dose nevirapine (NVP) regimen for prevention of mother-to-child transmission (PMTCT) of HIV in settings without the capacity to deliver more complex regimens, but the population-level impact of this intervention has rarely been assessed. Methods: A decision analysis model was developed, parameterized, and applied using local epidemiologic and demographic data to estimate vertical transmission of HIV and the impact of the PMTCT program in Zimbabwe up to 2005. Results: Between 1980 and 2005, of approximately 10 million children born in Zimbabwe, a cumulative 504,000 (range: 362,000 to 665,000) were vertically infected with HIV; 59% of these infections occurred in nonurban areas. Mother-to-child transmission (MTCT) of HIV decreased from 8.2% (range: 6.0% to 10.7%) in 2000 to 6.2% (range: 4.9% to 8.9%) in 2005, predominantly attributable to declining maternal HIV prevalence rather than to the PMTCT program. Between 2002 and 2005, the single-dose NVP PMTCT program may have averted 4600 (range: 3900 to 7800) infections. In 2005, 32% (range: 26% to 44%) and 4.0% (range: 2.7% to 6.2%) of infections were attributable to breast-feeding and maternal sero-conversion, respectively, and the PMTCT program reduced infant infections by 8.8% (range: 5.5% to 12.1%). Twice as many infections could have been averted had a more efficacious but logistically more complex NVP + zidovudine regimen been implemented with similar coverage (50%) and acceptance (42%). Discussion: The decline in MTCT from 2000 to 2005 is attributable more to the concurrent decrease in HIV prevalence in pregnant
women than to PMTCT at the current level of rollout. To improve the impact of PMTCT, program coverage and acceptance must be increased, especially in rural areas, and local infrastructure must then be strengthened so that single-dose NVP can be replaced with a more efficacious regimen.

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Abstr. Objectives: In developing countries, where mother-to-child transmission of HIV through breast-feeding is common, little is known about the impact of postpartum transmission on child survival. This study assessed whether children infected postpartum have longer survival from time of infection versus those infected during gestation or delivery. Design: We used a prospective cohort study to analyze data from 213 HIV-infected children enrolled in a breast-feeding intervention trial in Lusaka, Zambia (2001 to 2004). Methods: We compared mortality 1 year after HIV infection in children stratified by age of infection: 0 to 3 days (intrauterine [IU] group), 4 to 40 days (intrapartum/early postpartum [IP/EPP] group), and >40 days (postpartum [PP] group). Results: A total of 61, 71, and 81 children were infected in the IU, IP/EPP, and PP groups, respectively. Children with intrauterine or intrapartum/early postpartum transmission had higher mortality over the first 12 months after infection than children with postpartum transmission (P = 0.001 and P = 0.006, respectively); no differences were detected between children with intrauterine and intrapartum/early postpartum transmission. Nearly 20% of the IU and IP/EPP groups died by 100 days after infection, whereas nearly 10% of the PP group had died by this time. After adjusting for birth weight, maternal CD4 cell count, breast-feeding, and maternal death, children infected postpartum had one quarter the mortality rate (hazard ratio [HR] = 0.27, 95% confidence interval [CI]: 0.15 to 0.50) of those infected in utero. Stopping breast-feeding increased mortality in infected children (HR = 3.1, 95% CI: 1.8 to 5.3). Conclusions: This study demonstrates a survival benefit among children infected postpartum versus children infected during pregnancy or delivery and a benefit to increased breast-feeding duration among infected children. Testing children for HIV early may provide a means to allow for earlier intervention.

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**Abstr.** Background Malawi, which has about 80000 deaths from AIDS every year, made free antiretroviral therapy available to more than 80000 patients between 2004 and 2006. We aimed to investigate mortality in a population before and after the introduction of free antiretroviral therapy, and therefore to assess the effects of such programmes on survival at the population level. Methods We used a demographic surveillance system to measure mortality in a population of 32 000 in northern Malawi, from August, 2002, when free antiretroviral therapy was not available in the study district, until February, 2006, 8 months after a clinic opened. Causes of death were established through verbal autopsies (retrospective interviews). Patients who registered for antiretroviral therapy at the clinic were identified and linked to the population under surveillance. Trends in mortality were analysed by age, sex, cause of death, and zone of residence. Findings Before antiretroviral therapy became available in June, 2005, mortality in adults (aged 15-59 years) was 9.8 deaths for 1000 person-years of observation (95% CI 8.9-10.9). The probability of dying between the ages of 15 and 60 years was 43% (39-49) for men and 43% (38-47) for women; 229 of 352 deaths (65.1%) were attributed to AIDS. 8 months after the clinic that provided antiretroviral therapy opened, 107 adults from the study population had accessed treatment, out of an estimated 334 in need of treatment. Overall mortality in adults had decreased by 10% from 10.2 to 8.7 deaths for 1000 person-years of observation (adjusted rate ratio 0.90, 95% CI 0.70-1.14). Mortality was reduced by 35% (adjusted rate ratio 0.65, 0.46.0 .92) in adults near the main road, where mortality before antiretroviral therapy was highest (from 13.2 to 8.5 deaths per 1000 person-years of observation before and after antiretroviral therapy). Mortality in adults aged 60 years or older did not change. Interpretation Our findings of a reduction in mortality in adults aged between 15 and 59 years, with no change in those older than 60 years, suggests that deaths from AIDS were averted by the rapid scale-up of free antiretroviral therapy in rural Malawi, which led to a decline in adult mortality that was detectable at the population level.

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**Spectrum of adverse events after generic HAART in southern Indian HIV-infected patients.** AIDS Patient Care & Stds 2008;22(4):337-344.

**Abstr.** To determine the incidence of clinically significant adverse events after long-term, fixed-dose, generic highly active antiretroviral therapy (HAART) use among HIV-infected individuals in South India, we examined the experiences of 3154 HIV-infected individuals who received a minimum of 3 months of generic HAART between February 1996 and December 2006 at a tertiary HIV care referral center in South India. The most common regimens were 3TC + d4T + nevirapine (NVP) (54.8%), zidovudine (AZT) + 3TC + NVP (14.5%), 3TC + d4T + efavirenz (EFV) (20.1%), and AZT + 3TC + EFV (5.4%). The most common adverse events and median CD4 at time of event were rash (15.2%; CD4, 285 cells/μL) and peripheral neuropathy (9.0% and 348 cells/μL). Clinically significant anemia (hemoglobin < 7 g/dL) was observed in 5.4% of patients (CD4, 165 cells/μL) and hepatitis (clinical jaundice with alanine aminotransferase > 5 times upper limits of normal) in 3.5% of patients (CD4, 260 cells/μL). Women were significantly more likely to experience lactic acidosis, while men were significantly more likely to experience immune reconstitution syndrome (p < 0.05). Among the patients with 1 year...
of follow-up, NVP therapy was significantly associated with developing rash and d4T therapy with developing peripheral neuropathy (p < 0.05). Anemia and hepatitis often occur within 12 weeks of initiating generic HAART. Frequent and early monitoring for these toxicities is warranted in developing countries where generic HAART is increasingly available.

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**Selection of text.** The aim of this article is to review the state of knowledge in the field of paediatric HIV/AIDS, to describe the research undertaken over the past decade, and to assess the level of implementation of research results, focusing mainly on the experience of African countries. During the past two decades, international efforts to fight against HIV/AIDS have yielded important research successes for child survival in LINCs. However the transition from research to action remains largely insufficient. Improving the coverage of PMTCT should be a priority. There is also enough evidence today to roll out paediatric HIV care and treatment, at least at the same speed and extent than adult care. This however requires improving health care systems as well as political commitment and funding at international and national levels. Current knowledge indicates that orphans and vulnerable children pay a large tribute to HIV/AIDS and deserve a large-scale response. Finally, the fight against HIV/AIDS requires the scaling-up and intensification of primary HIV prevention, as part of a comprehensive response that simultaneously expands access to treatment and care.

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**Abstr.** Background In lower-income countries, WHO recommends a population-based approach to antiretroviral treatment with standardised regimens and clinical decision making based on clinical status and, where available CD4 cell count, rather than viral load. Our aim was to study the potential consequences of such monitoring strategies, especially in terms of survival and resistance development. Methods A validated computer simulation model of HIV infection and the effect of antiretroviral therapy was used to compare survival, use of second-line regimens, and development of resistance that result from different strategies—based on viral load, CD4 cell count, or clinical observation alone—for determining when to switch people starting antiretroviral treatment with the WHO-recommended first-line regimen of stavudine, lamivudine, and nevirapine to second-line antiretroviral treatment. Findings Over 5 years, the predicted proportion of potential life-years survived was 83% with viral load monitoring (switch when viral load >500 copies per mL), 82% with CD4 cell count monitoring (switch at 50% drop from peak), and 82% with clinical monitoring (switch when two new WHO stage 3 events or a WHO stage 4 event occur). Corresponding values over 20 years were 67%, 64%, and 64%. Findings were robust to variations in model specification in extensive univariable and multivariable sensitivity analyses. Although survival was slightly longer with viral load monitoring, this strategy was not the most cost effective. Interpretation For patients on the first-line regimen of stavudine, lamivudine, and nevirapine the benefits of viral
load or CD4 cell count monitoring over clinical monitoring alone are modest. Development of cheap and robust versions of these assays is important, but widening access to antiretrovirals-with or without laboratory monitoring—is currently the highest priority.

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Abstr. Objective: To assess the rates and determinants of mortality, loss to follow-up and immunological failure in a nongovernmental organization-implemented program of access to antiretroviral treatment in Cote d'Ivoire. Methods: In each new treatment center, professionals were trained in HIV care, and a computerized data system was implemented. Individual patient and program level determinants of survival, loss to follow-up and immunological failure were assessed by multivariate analysis. Results: Between May 2004 and February 2007, 10211 patients started antiretroviral treatment in 19 clinics (median preantiretroviral treatment CD4 cell count, 123 cells/µl; initial regimen zidovudine-lamivudine-efavirenz, 20%; stavudine-lamivudine-efavirenz, 22%; stavudine-lamivudine-nevirapine, 52%). At 18 months on antiretroviral treatment, the median gain in CD4 cell count was +202 cells/µl, the probability of death was 0.15 and the probability of being loss to follow-up was 0.21. In addition to the commonly reported determinants of impaired outcomes (low CD4 cell count, low BMI, low hemoglobin, advanced clinical stage, old age and poor adherence), two factors were also shown to independently jeopardize prognosis: male sex (men vs. women: hazard ratio = 1.52 for death, 1.27 for loss to follow-up, 1.31 for immunological failure); and attending a recently opened clinic (inexperienced vs. experienced centers: hazard ratio = 1.40 for death, 1.58 for loss to follow-up). None of the three outcomes was associated with the drug regimen. Discussion: In this rapidly scaling-up program, survival and immune reconstitution were good; women and patients followed up in centers with longer experience had better outcomes; outcomes were similar in zidovudine/stavudine-based regimens and in efavirenz/nevirapine-based regimens. Decreasing the rate of loss to follow-up should now be the top priority in antiretroviral treatment rollout.

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Abstr. Objective: Mulago and Mbarara hospitals are large tertiary hospitals in Uganda with a high HIV/AIDS burden. Until recently, HIV testing was available only upon request and payment. From November 2004, routine free HIV testing and counselling has been offered to improve testing coverage and the clinical management of patients. All patients in participating units who had not previously tested HIV-positive were offered HIV testing. Family members of patients seen at the hospitals were also offered testing. Methods: Data collected at the 25 participating wards and clinics between 1 November 2004 and 28 February 2006 were analysed to determine the uptake rate of testing and the HIV seroprevalence among patients and their family members. Findings: Of the 51 642 patients offered HIV testing, 50 649 (98%) accepted. In those who had not
previously tested HIV-positive, the overall HIV prevalence was 25%, with 81% being tested for the first time. The highest prevalence was found in medical inpatients (35%) and the lowest, in surgical inpatients (12%). The prevalence of HIV was 28% in the 39,037 patients who had never been tested before and 9% in those who had previously tested negative. Of the 10,439 family members offered testing, 9,720 (93%) accepted. The prevalence in family members was 20%. Among 1213 couples tested, 224 (19%) had a discordant HIV status. Conclusion In two large Ugandan hospitals, routine HIV testing and counselling was highly acceptable and identified many previously undiagnosed HIV infections and HIV-discordan t partnerships among patients and their family members.

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Selection of text. Last week, the World Bank launched a new agenda for action on HIV/AIDS in Africa for the next 5 years, with four main objectives: to advise countries on the management of international financing, help countries to take a development response to HIV/AIDS, strengthen the monitoring capacity of countries to track the effectiveness of their response, and build stronger health systems. The new agenda follows on from the Bank’s Africa Multi-Country AIDS Program (MAP), which was launched in 2000. MAP was the first programme to offer African countries long-term funding for national HIV programmes. MAP supported multisectorial approaches to combat HIV/AIDS and was the strongest mechanism in funding to create the infrastructure for national AIDS councils. However, MAP’s impact on HIV/AIDS is unclear. A few years after its launch other big funders, such as the Global Fund to Fight AIDS, Tuberculosis and Malaria, came onto the scene. Implicit in their creation was the fact that MAP was not working. What about the new strategy? The Bank is continuing its unique multisectoral approach. It plans to disburse US$250 million a year for HIV/AIDS initiatives in health, education, and transport. This investment is a welcome move. However, to be effective, the Bank’s lending should be based on good performance and not left to the whimsy of individuals within the organisation. What is more, the Bank has lacked and continues to lack top-level political commitment to HIV/AIDS in Africa. The new strategy was not signed or launched by the Bank’s new head, Robert Zoellick. It also speaks volumes that the agenda was not released at one of the many upcoming high-level HIV meetings. The Bank must have a coherent, performance-based strategy with strong political support from its new leader if it is to make a real contribution to addressing HIV/AIDS. Its latest effort lacks that necessary commitment to a disease that remains an overwhelming threat.

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