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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** (Written by the Bordeaux Working Group). **Author Address**, if available, **Free Full Text**, if available

Bolton Moore C, Mubiana Mbewe M, Cantrell RA, Chintu N, Stringer EM, Chi BH, Sinkala M, Kankasa C, Wilson CM, Wilfert CM, Mwango A, Levy J, Abrams EJ, Bulterys M, Stringer JSA. **Clinical outcomes and CD4 cell response in children receiving antiretroviral therapy at primary health care facilities in Zambia.** Journal of the American Medical Association 2007;298(16):1888-1899.

Abstr. Context The Zambian Ministry of Health provides pediatric antiretroviral therapy (ART) at primary care clinics in Lusaka, where, despite scale-up of perinatal prevention efforts, many children are already infected with the human immunodeficiency virus (HIV). Objective To report early clinical and immunologic outcomes of children enrolled in the pediatric treatment program. Design, Setting, and Patients Open cohort assessment using routinely collected clinical and outcome data from an electronic medical record system in use at 18 government primary health facilities in Lusaka, Zambia. Care was provided primarily by nurses and clinical officers ("physician extenders" akin to physician assistants in the United States). Patients were children (< 16 years of age) presenting for HIV care between May 1, 2004, and June 29, 2007. Intervention Three-drug ART (zidovudine or stavudine plus lamivudine plus nevirapine or efavirenz) for children who met national treatment criteria. Main Outcome Measures Survival, weight gain, CD4 cell count, and hemoglobin response. Results After enrollment of 4975 children into HIV care, 2938 (59.1%) started ART. Of those initiating ART, the median age was 81 months (interquartile range, 36-125), 1531 (52.1%) were female, and 2087 (72.4%) with World Health Organization stage information were in stage III or IV. At the time of analysis, 158 children (5.4%) had withdrawn from care and 382 (13.0%) were at least 30 days late for follow-up. Of the remaining 2398 children receiving ART, 198 (8.3%) died over 3018 child-years of follow-up (mortality rate, 6.6 deaths per 100 child-years; 95% confidence interval [CI], 5.7-7.5); of these deaths, 112 (56.6%) occurred within 90 days of therapy initiation (early mortality rate, 17.4/100 child-years; post-90-day mortality rate, 2.9/100 child-years). Mortality was associated with CD4 cell depletion, lower weight-for-age, younger age, and anemia in multivariate analysis. The mean CD4 cell percentage at ART initiation among the 1561 children who had at least 1 repeat measurement was 12.9% (95% CI, 12.5%-13.3%) and increased to 23.7% (95% CI, 23.1%-24.3%) at 6 months, 27.0% (95% CI, 26.3%-27.6%) at 12 months, 28.0% (95% CI, 27.2%-28.8%) at 18 months, and 28.4% (95% CI, 27.4%-29.4%) at 24 months. Conclusions Care provided by clinicians such as nurses and clinical officers can result in good outcomes for HIV-infected children in primary health care settings in sub-Saharan Africa. Mortality during the first 90 days of therapy is high, pointing to a need for earlier intervention.

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Free Full Text: <http://jama.ama-assn.org/cgi/reprint/298/16/1888>

Chi BH, Sinkala M, Mbewe F, Cantrell RA, Kruse G, Chintu N, Aldrovandi GM, Stringer EM, Kankasa C, Safrit JT, Stringer JSA. **Single-dose tenofovir and emtricitabine for reduction of viral resistance to non-nucleoside reverse transcriptase inhibitor drugs in women given intrapartum nevirapine for perinatal HIV prevention: an open-label randomised trial.** Lancet 2007;370(9600):1698-1705.

Abstr. Background Intrapartum and neonatal single-dose nevirapine are essential components of perinatal HIV prevention in resource-constrained settings, but can induce resistance to other non-nucleoside reverse transcriptase inhibitor drugs. We aimed to investigate whether this complication would be reduced with a single peripartum intervention of tenofovir and emtricitabine. Methods We randomly assigned 400 HIV-infected pregnant women who sought care at two public-sector primary health facilities in Lusaka, Zambia. One was excluded, 200 were assigned to receive a single oral dose of 300 mg tenofovir disoproxil fumarate with 200 mg emtricitabine under direct observation, and 199 to receive no study drug. Short-course zidovudine and intrapartum nevirapine were offered to all HIV-infected women, according to the local standard of

care. Women who met national criteria for antiretroviral therapy were referred for care and not enrolled. Our primary study outcome was resistance to non-nucleoside reverse transcriptase inhibitors at 6 weeks after delivery. We used standard population sequencing to determine HIV genotypes. Analysis was per protocol. This study is registered with ClinicalTrials.gov, number NCT00204308. Findings Of the 200 women who were randomly assigned to the intervention, 14 were lost to follow-up or withdrew from the study, two did not take study drug according to protocol, and one specimen was lost; 23 of 199 controls were lost to follow-up or withdrew from the study, and three specimens were lost. Women given the intervention were 53% less likely than controls to have a mutation that conferred resistance to non-nucleoside reverse transcriptase inhibitors at 6 weeks after delivery (20/173 [12%] vs 41/166 [25%]; risk ratio [RR] 0.47, 95% CI 0.29-0.76). We noted postpartum anaemia, the most common serious adverse event in mothers, in four women in each group. 20 of 198 (10%) infants in the intervention group and 23 of 199 (12%) controls had a serious adverse event, mostly due to septicaemia (n=22) or pneumonia (n=8); these events did not differ between groups, and none were judged to be caused by the study intervention. Interpretation A single dose of tenofovir and emtricitabine at delivery reduced resistance to non-nucleoside reverse transcriptase inhibitors at 6 weeks after delivery by half, therefore this treatment should be considered as an adjuvant to intrapartum nevirapine.

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Kitchener H, Nelson L, Adams J, Mesher D, Sasieni P, Cubie H, Moore C, Heard I, Agarossi A, Denny L, Bradbeer C. **Colposcopy is not necessary to assess the risk to the cervix in HIV-positive women: An international cohort study of cervical pathology in HIV-1 positive women.** International Journal of Cancer 2007;121(11):2484-2491.

Abstr. The objectives of this prospective multicentre international cohort study are to describe the characteristics of a cohort of HIV-1 positive women and determine the best management system by comparing cervical pathology according to results of cytology, colposcopy and human papillomavirus (HPV) testing at baseline and throughout follow-up. A. Cohorts of known HIV-positive women were recruited from 6 hospital-based European centres and a community-based South African Centre. Following registration, women were reviewed every 6 months to undergo cervical surveillance including cytology, colposcopy, histopathology and HPV testing, using the HPV hybrid capture assay. Independent risk factors for the incidence of cytological abnormality and acquisition/ clearance of HPV infection during follow up were identified. A total of 1,534 women were recruited, 400 of which were from South Africa. At baseline, among European women, 66% had normal cytology and half were HPV negative and among South African women, 45% had normal cytology and one third (32%) were HPV negative. The sensitivity of cytology (\geq ASCUS) matched with that of colposcopy to detect CIN2+. Rate of detection of high grade CIN at 2 years was similar in European and South African women (11 and 9.3%, respectively). Cytology and HPV testing alone were each sufficiently sensitive as a screening test at 2 yearly intervals. Our data confirm the high prevalence of low-grade cytological abnormalities and high-risk HPV infection. Cytology appears to be sufficient for cervical surveillance, with HPV testing being less specific with poor positive predictive value. There appears to be no additional benefit from routine colposcopy.

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Lockman S, McIntyre JA. **Reduction of HIV-1 drug resistance after intrapartum single-dose nevirapine [Comment]**. *Lancet* 2007; 370(9600):1668-1670.

Full Text: Few issues in mother-to-child HIV-1 transmission have sparked as much controversy as intrapartum single-dose nevirapine. This drug is 40% efficacious in the prevention of such transmission, easy to use, safe, and cheap, which are all especially important in the developing world, where half a million children are infected annually by this route. But, by 2006, only 11% of HIV-infected women in sub-Saharan Africa were receiving antiretroviral drugs to prevent transmission to their children. The obstacles there include limited antenatal care: only two-thirds of pregnant women have at least one antenatal visit with a nurse or doctor, and under half have four or more. However, single-dose nevirapine programmes can be effectively implemented in these settings. After single-dose nevirapine, 19–75% of women and 33–87% of the minority of infants who become infected and develop virus that is resistant to non-nucleoside reverse-transcriptase inhibitors (NNRTIs). Combination of other antiretrovirals with single-dose nevirapine somewhat attenuates the emergence of nevirapine resistance. The TOPS study from South Africa showed that addition of intrapartum plus 4–7 days of maternal postpartum zidovudine/lamivudine significantly reduced detectable nevirapine resistance (from 57% to 9–13%) in women who did not receive any antenatal antiretrovirals. NNRTIs are a component of first-line antiretroviral regimens throughout the world. Resistance that arises after single-dose nevirapine can compromise response to subsequent maternal treatment with nevirapine-based antiretrovirals, and although the problem is less in women who start antiretrovirals 6 or more months after taking single-dose nevirapine, and Maternal combination prophylaxis regimens are also more effective at preventing vertical transmission than is single-dose nevirapine alone, and some practitioners therefore believe the latter should not be used at all—even though it may be the only feasible intervention in many areas. In today's *Lancet*, Benjamin Chi and colleagues present new and encouraging data from Zambia to show that addition of one intrapartum dose of tenofovir/emtricitabine to short-course zidovudine plus single-dose nevirapine significantly reduced the prevalence of detectable nevirapine-resistant maternal virus at 6 weeks' postpartum. In the subgroup of women with sequences available for analysis at 6 weeks' postpartum, 30% of 138 women in the control group compared with 14% of 147 women in the intervention group harboured nevirapine-resistant virus. Importantly, mutations associated with resistance to tenofovir or emtricitabine were not detected at any time. In Chi and colleagues' study, only women with less advanced HIV-1 disease (who did not qualify for combination antiretrovirals) were eligible to enter. Also, 81% of participants also took short-course zidovudine (for a median of about 37 days) before single-dose nevirapine (in either group). Both these factors might have reduced the median maternal HIV-1 RNA levels at delivery. Because higher HIV-1 RNA at delivery has been associated with greater risk for selection of resistance after single-dose nevirapine, the relative risk of developing nevirapine resistance might be different in settings in which women do not have access to or present too late in pregnancy to receive antenatal antiretrovirals (as recommended by WHO22 and used by Chi). Chi and colleagues classified maternal samples with HIV-1 RNA levels below 2000 copies per mL (not genotyped due to low yield) as harbouring no resistance in the primary analysis, rather than omitting them from the analysis altogether as would generally be done. The analysis as done could lead to underestimation of the prevalence of resistance, particularly in the intervention group at 2 weeks, in view of the transient suppression of viral load that was associated with being on tenofovir/emtricitabine. The secondary analysis which omitted samples that were not genotyped might be more valid. We also need to learn about the incidence of nevirapine resistance in infants who become HIV-1 infected despite the addition of tenofovir/emtricitabine to zidovudine and single-dose nevirapine. Since Chi and colleagues' study was conceived, new data have somewhat allayed concerns about the clinical implications of maternal nevirapine resistance after single-dose nevirapine, but resistance in HIV-infected infants may have more dire implications for subsequent paediatric response to nevirapine-based treatment. Additionally, although the clinical implications of minority resistant variant populations are unknown, future studies of the

presence of such variants after the addition of single-dose tenofovir/emtricitabine will be important, particularly to assess for resistance to emtricitabine. It would be of concern if the use of single doses of both tenofovir/emtricitabine and nevirapine resulted in large proportions of patients developing even low-level resistance to both emtricitabine and nevirapine, which might affect subsequent response to treatment with these commonly used classes of drugs. Finally, although it is unlikely that one dose of tenofovir given to a mother and newborn infant is associated with important toxic effects in infants (including adverse effects on bone development), the safety of in-utero exposure to tenofovir is being examined. The question today is under what circumstances single-dose tenofovir/emtricitabine should be used as part of a regimen to prevent mother-to-child transmission of HIV, in view of Chi and colleagues' data. Combination three-drug prophylaxis might in the future be increasingly available to all pregnant HIV-1-infected women regardless of CD4+ cell count, which would make single-dose nevirapine obsolete. Currently, however, most women either do not receive any intervention at all, or take only single-dose nevirapine. Chi's results cannot necessarily be extrapolated to women who take only nevirapine without antenatal zidovudine, for the reasons noted above. However, WHO recommends that women with less advanced HIV (who comprise the majority of HIV-infected pregnant women) be given short-course zidovudine with single-dose nevirapine (with a 7-day "tail" of zidovudine plus lamivudine). Chi's results do provide strong evidence that addition of single-dose tenofovir/emtricitabine to short-course zidovudine and single-dose nevirapine in women with higher CD4+ cell counts is a new, effective, and feasible approach to reducing maternal nevirapine resistance, and one that should be seriously considered for implementation.

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Obermeyer CM, Osborn M. **The utilization of testing and counseling for HIV: A review of the social and behavioral evidence.** American Journal of Public Health 2007;97(10):1762-1774.

Abstr. Against the background of debates about expanding HIV testing and counseling, we summarize the evidence on the social and behavioral dimension of testing and its implications for programs. The discrepancy between acceptance of testing and returning for results and the difficulties of disclosure are examined in light of research on risk perceptions and the influence of gender and stigma. We also summarize the evidence on the provision of testing and counseling, the implementation of practices regarding confidentiality and consent, and the results of interventions. We demonstrate that social factors have a considerable impact on testing, show that the services linked to testing are key determinants of utilization, and consider the implications of these findings for HIV testing programs.

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Pirillo MF, Bassani L, Germinario EAP, Mancini MG, Vyankandondera J, Okong P, Vella S, Giuliano M. **Seroprevalence of hepatitis B and C viruses among HIV-Infected pregnant women in Uganda and Rwanda.** Journal of Medical Virology 2007;79(12):1797-1801.

Abstr. A retrospective survey to estimate the prevalence of hepatitis B (HBV) and C (HCV) infections was conducted on the samples of 247 African HIV-1 positive pregnant women who had participated to a mother-to-child prevention trial carried out in urban settings in Kampala, Uganda and Kigali, Rwanda. Hepatitis B markers studied were HBs antigen (HBsAg) and, if positive after confirmatory testing, HBe antigen/anti-HBe antibodies and HBV DNA. A fourth generation HCV enzyme immunoassay (EIA) was used for primary HCV screening. Positive samples were analyzed further with a second different EIA. Both for HBV and for HCV the use of confirmatory tests allowed the removal of frequent false-positive screening results. HBsAg was found in 10/246 women

(seroprevalence 4.1%, 95% confidence interval (95%CI) 1.7-6.8):8/164 (4.9%) in Uganda and 2/82 (2.4%) in Rwanda. HBe Ag was found in 33% of HBsAg-positive patients and HBV DNA was quantifiable in 71%. Anti-HCV antibodies were found in 5/247 women (seroprevalence 2.0% 95%CI 0.3-3.9): 1/165 (0.6%) in Uganda and 4/82 (4.9%) in Rwanda. There was no interrelation between HCV and HBV markers. There was no difference between patients with and without co-infection with HBV or HCV with regards to CD4+ cell count. Overall, hepatitis B and C co-infection was relatively infrequent in this group of pregnant women. However, since approximately 6% of HIV-positive women in these countries had a co-infection with one hepatitis virus, caution should be used in the monitoring of possible hepatotoxicity related to antiretroviral drugs in these populations.

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UNAIDS, WHO. AIDS Epidemic Update. Geneva: UNAIDS; 2007. Report No.: UNAIDS/07.27E.

Free Full Text: http://data.unaids.org/pub/EPISlides/2007/2007_epiupdate_en.pdf

UNICEF. Progress for Children: A World Fit for Children Statistical Review (No. 6). New York: UNICEF; 2007.

Free Full Text: http://www.unicef.org/publications/files/Progress_for_Children_No_6.pdf

UNICEF. Children and the Millennium Development Goals: Progress towards A World Fit for Children. New York: UNICEF; 2007.

Free Full Text: http://www.unicef.org/publications/files/Children_and_the_MDGs.pdf

UNICEF. A World Fit For Us: The Children's Statement from the UN Special Session on Children: Five years on. New York: UNICEF; 2007.

Free Full Text: http://www.unicef.org/publications/files/A_World_Fit_for_Us.pdf