



HIV Care & PMTCT in Resource-Limited Settings

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prepared by the Bordeaux Working Group

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Number of citations selected for this issue: 24

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**

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)

Bentley ME, Corneli AL, Piwoz E, Moses A, Nkhoma J, Tohill BC, Ahmed Y, Adair L, Jamieson DJ, van der Horst C. **Perceptions of the role of maternal nutrition in HIV-positive breast-feeding women in Malawi.** *Journal of Nutrition* 2005;135(4):945-949.

Abstr. A neglected issue in the literature on maternal nutrition and HIV is how HIV-positive women perceive their own bodies, health, and well-being, particularly in light of their infection, and whether these perceptions influence their infant feeding practices and their perceived ability to breast-feed exclusively through 6 mo. We conducted formative research to better understand breast-feeding practices and perceptions, and to inform the Breastfeeding, Antiretroviral, and Nutrition (BAN) Study, a clinical trial to evaluate antiretroviral and nutrition interventions to reduce mother-to-child transmission of HIV during breast-feeding in Lilongwe, Malawi. Twenty-two HIV-positive women living in semirural areas on the periphery of Lilongwe participated in in-depth interviews. In an adaptation of the body-silhouette methodology, nine culturally appropriate body silhouettes, representing a continuum of very thin to very large shapes, were used to elicit women's views on their present, previous-year, and preferred body shapes, and on the shape they perceived as healthy. The narrative scenario method was also used to explore women's views on 2 fictional women infected with HIV and their ability to exclusively breast-feed. Women perceived larger body shapes as healthy, because fatness is considered a sign of good health and absence of disease, and many recognized the role of nutrition in achieving a preferred or healthy body shape. Several women believed their nutritional status (body size) was declining because of their illness. Women were concerned that breast-feeding may increase the progression of HIV, suggesting that international guidelines to promote appropriate infant feeding practices for infants whose mothers are infected with HIV should focus on the mother's health and well-being, as well as the infant's.

Note: Five other articles relevant to child nutrition & HIV in resource-limited settings were published in the same issue of *Journal of Nutrition*, including the paper by Piwoz and Bentley quoted below.

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Infant feeding / Breastfeeding, LICs / Africa

Chopra M, Doherty T, Jackson D, Ashworth A. **Preventing HIV transmission to children: Quality of counselling of mothers in South Africa.** *Acta Paediatrica* 2005;94(3):357-363.

Abstr. Aim: To assess the quality of counselling provided to mothers through the programme to prevent mother-to-child transmission (PMTCT) of HIV in South Africa. Methods: Structured observations of consultations and exit interviews with 60 mothers attending clinics at three purposively selected PMTCT sites across South Africa were conducted. Results: Twenty-two counsellors were observed. The general quality of communication skills was very good, and 73% of HIV-negative mothers were informed of the advantages of exclusive breastfeeding (EBF). However, only one of 34 HIV-positive mothers was informed about the possible side effects of nevirapine, and none was told what to do when it occurred. Only two HIV-positive mothers were asked about essential conditions for safe formula feeding before a decision about an infant feeding option was made. None of the 12 mothers choosing to breastfeed was shown how to position the baby correctly on the breast or asked whether they thought EBF was feasible. Fewer than a quarter of mothers expressed confidence in performing the actions required, and 85% could not define the term EBF. Conclusion: The poor quality of counselling in the PMTCT programme will reduce the effectiveness of these programmes. As they are being scaled up, there needs to be far more attention paid towards the counselling of mothers, especially with regards to optimal infant feeding.

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LICs / Africa, PMTCT, VCT

Chu JH, Gange SJ, Anastos K, Minkoff H, Cejtin H, Bacon M, Levine A, Greenblatt RM. **Hormonal contraceptive use and the effectiveness of highly active antiretroviral therapy.** *American Journal of Epidemiology* 2005;161(9):881-890.

Abstr. The role of hormonal contraceptive use in the effectiveness of highly active antiretroviral therapy (HAART) was examined among participants in the Women's Interagency HIV Study who were followed from HAART initiation to 2001. Propensity score selection was used to match 77 hormonal contraceptive users with 77 nonusers on age, race, and pre-HAART CD4-positive T-lymphocyte (CD4+ cell) count and viral load. The authors compared hormonal contraceptive users and nonusers with regard to the CD4+ cell count and viral load responses to HAART upon initiation. Proportional hazards analyses were used to assess the effect of hormonal contraceptive use on times to increases in CD4+ cell count of 50 cells/mm³ and 100 cells/mm³ and achievement of an undetectable viral load. There were no statistically significant differences in CD4+ cell counts and log viral load responses by hormone use after HAART initiation, except in log viral load at the third visit after initiation (p = 0.047). Time-dependent hormonal contraceptive use was not a statistically significant predictor of achieving increases in CD4+ cell count of 50 cells/mm³ and 100 cells/mm³ or an undetectable

viral load ($p = 0.517$, $p = 0.751$, and $p = 0.218$, respectively) after HAART initiation. In conclusion, the authors did not find substantial evidence that use of hormonal contraceptives strongly affected responses to HAART.

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Adults / Women, Contraception, HAART, Industrialized countries

Couzin J. **AIDS research - IOM panel clears HIV prevention study.** Science 2005;308(5720):334.

An Institute of Medicine (IOM) panel has found no major improprieties in the conduct of a key HIV trial in Uganda to prevent mother-to-child transmission in the late 1990s, essentially validating the use of a cheap, effective, and simple anti-HIV drug: nevirapine. The report also helps clear the names of Johns Hopkins University pathologist Brooks Jackson and more than a dozen colleagues. In two papers published in *The Lancet* in 1999 and 2003, National Institutes of Health (NIH)-funded researchers reported that giving a pregnant woman a single dose of nevirapine, and her infant a single dose immediately after birth, dramatically cut mother-to-child transmission rates. Since then, nevirapine has become the cornerstone of HIV prevention efforts in infants across Africa and beyond. But last year the work came under fire from an NIH staffer, Jonathan Fishbein, who charged that the investigators failed to adhere to regulatory standards governing data collection and record keeping (*Science*, 24 December 2004, p. 2168). He argued in an interview that "you cannot use this trial as part of the knowledge about how that drug works." The nine-member IOM committee agreed that the study wasn't foolproof. But "we feel firmly that the findings and the conclusion ... are valid," said committee member Mark Kline, a pediatric infectious disease specialist at Baylor College of Medicine in Houston, Texas. The committee had primary medical records sent from Uganda and focused on a sampling of 49 infants in the study. About 10% of adverse events went unreported in that sample, they noted. Fishbein immediately blasted the IOM report as "an apologist's statement" that supported NIH's point of view. At a tense press conference, he and his brother, Rand Fishbein, a defense and foreign policy consultant, asked how the IOM committee could be unbiased, given that six of its members receive NIH grants. IOM president Harvey Fineberg called that accusation "preposterous," adding that "there is nothing financially at stake for the individuals on this committee." Some in the AIDS prevention field, who have worried that African governments would abandon nevirapine, are hoping that the IOM report will end the controversy. The Ugandan trial "was a critical pilot study" of nevirapine that has been confirmed by at least a half-dozen others, says Arthur Ammann, a pediatric immunologist and president of Global Strategies for HIV Prevention in San Francisco.

Note: The report intitled *Review of the HIVNET 012 Perinatal HIV Prevention Study (2005)* is available at: <http://www.nap.edu/books/0309096510/html>

LICs / Africa, PMTCT / ARV, RCT

Ehrnst A, Zetterstrom R. **Feeding practices of HIV-1-infected mothers: The role of counsellors.** Acta Paediatrica 2005;94(3):263-265.

Abstr. In this issue of Acta Paediatrica, Chopra et al. report that voluntary counselling is central to preparing mothers for making a proper informed choice about adequate feeding practices to prevent their infants from acquiring HIV infection. The recommendations given and the way in which counselling is performed are the most important determinants of a mother's decision about how to feed her infant. In this article, we summarize the main arguments for and against breastfeeding by HIV-infected mothers. Conclusions: Further studies are needed to determine the alternatives to breastfeeding in countries where there is no access to safe formula feeding or to antiretroviral drugs. HIV-positive mothers should be made aware of the available feeding alternatives through adequate counselling from properly trained persons.

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Infant feeding / Breastfeeding, VCT

Iliff PJ, Piwoz EG, Tavengwa NV, Zunguza CD, Marinda ET, Nathoo KJ, Moulton LH, Ward BJ, Humphrey JH. **Early exclusive breastfeeding reduces the risk of postnatal HIV-1 transmission and increases HIV-free survival.** AIDS 2005;19(7):699-708.

Abstr. Objectives: The promotion of exclusive breastfeeding (EBF) to reduce the postnatal transmission (PNT) of HIV is based on limited data. In the context of a trial of postpartum vitamin A supplementation, we provided education and counseling about infant feeding and HIV, prospectively collected information on infant feeding practices, and measured associated infant infections and deaths. Design and methods: A total of 14 110 mother-newborn pairs were enrolled, randomly assigned to vitamin A treatment group after delivery, and followed for 2 years. At baseline, 6 weeks and 3 months, mothers were asked whether they were still breastfeeding, and whether any of 22 liquids or foods had been given to the infant. Breastfed infants were classified as exclusive, predominant, or mixed breastfed. Results: A total of 4495 mothers tested HIV positive at baseline; 2060 of their babies were alive, polymerase chain reaction negative at 6 weeks, and provided complete feeding information.

All infants initiated breastfeeding. Overall PNT (defined by a positive HIV test after the 6-week negative test) was 12.1%, 68.2% of which occurred after 6 months. Compared with EBF, early mixed breastfeeding was associated with a 4.03 (95% CI 0.98, 16.61), 3.79 (95% CI 1.40-10.29), and 2.60 (95% CI 1.21-5.55) greater risk of PNT at 6, 12, and 18 months, respectively. Predominant breastfeeding was associated with a 2.63 (95% CI 0.59-11.67), 2.69 (95% CI 0.95-7.63) and 1.61 (95% CI 0.72-3.64) trend towards greater PNT risk at 6, 12, and 18 months, compared with EBF. Conclusion: EBF may substantially reduce breastfeeding-associated HIV transmission. © 2005 Lippincott Williams and Wilkins.

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Infant feeding / Breastfeeding, LICs / Africa, MTCT

Jevtovic D, Salemovic D, Ranin J, Pesic I, Zerjav S, Djurkovic Djakovic O. **The prevalence and risk of immune restoration disease in HIV-infected patients treated with highly active antiretroviral therapy.** HIV Medicine 2005;6(2):140-143.

Abstr. Background It is becoming increasingly clear that, during successful highly active antiretroviral therapy (HAART), a proportion of treated patients develop opportunistic infections (OIs), referred to in this setting as immune restoration disease (IRD). We examined the risk of developing IRD in HAART-treated HIV-infected patients. Methods A retrospective study of a cohort including all 389 patients treated with HAART between 1 January 1998 and 31 May 2004 in our HIV unit was performed to evaluate the occurrence of and risk factors for IRD during HAART. Baseline and follow-up values of CD4 T-cell counts and plasma viral loads (pVLs) were compared to assess the success of HAART. Results During successful HAART (significant increase in CD4 T-cell counts and decrease in pVL), at least one IRD episode occurred in 65 patients (16.7%). The median time to IRD was 4.6 months (range 212 months). IRDs included dermatomal herpes zoster (26 patients), pulmonary tuberculosis (four patients), tuberculous exudative pericarditis (two patients), tuberculous lymphadenitis (two patients), cerebral toxoplasmosis (one patient), progressive multifocal leucoencephalopathy (PML) (one patient), inflamed molluscum (one patient), inflamed Candida albicans angular cheilitis (three patients), genital herpes simplex (two patients), tinea corporis (two patients), cytomegalovirus (CMV) retinitis (two patients), CMV vitritis (one patient) and hepatitis B (three patients) or C (fifteen patients). A baseline CD4 T-cell count below 100 cells/ μ mL was shown to be the single predictor [odds ratio (OR) 2.5, 95% confidence interval (CI) 0.9-6.4] of IRD, while a CD4 T-cell count increase to > 400 cells/ μ mL, but not undetectable pVL, was a negative predictor of IRD (OR 0.3, 95% CI 0.1-0.8). Conclusions To avoid IRD in advanced patients, HAART should be initiated before the CD4 T-cell count falls below 100 cells/ μ mL.

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Eastern Europe, HAART, Treatment complications

Konopnicki D, Mocroft A, de Wit S, Antunes F, Ledergerber B, Katlama C, Zilmer K, Vella S, Kirk O, Lundgren JD. **Hepatitis B and HIV: prevalence, AIDS progression, response to highly active antiretroviral therapy and increased mortality in the EuroSIDA cohort.** AIDS 2005;19(6):593-601.

Abstr. Background: Whether hepatitis B (HBV) coinfection affects outcome in HIV-1-infected patients remains unclear. Objective: To assess the prevalence of HBV (assessed as HBsAg) coinfection and its possible impact on progression to AIDS, all-cause deaths, liver-related deaths and response to highly active antiretroviral therapy (HAART) in the EuroSIDA cohort. Methods: Data on 9802 patients in 72 European HIV centres were analysed. Incidence rates of AIDS, global mortality and liver-related mortality, time to 25% CD4 cell count increase and time to viral load < 400 copies/ml after starting HAART were calculated and compared between HBsAg-positive and HBsAg-negative patients. Results: HBsAg was found in 498 (8.7%) patients. The incidence of new AIDS diagnosis was similar in HBsAg-positive and HBsAg-negative patients (3.3 and 3.4/100 person-years, respectively) even after adjustment for potential confounders: the incidence rate ratio (IRR) was 0.94 [95% confidence interval (CI), 0.74-1.19; P=0.61]. The incidences of all-cause and liver-related mortalities were significantly higher in HBsAg-positive subjects (3.7 and 0.7/100 person-years, respectively) compared with HBsAg-negative subjects (2.6 and 0.2/100 person-years, respectively). The adjusted IRR values were 1.53 for global (95% CI, 1.23-1.90; P = 0.0001) and 3.58 for liver-related (95% CI, 2.09-6.16; P < 0.0001) mortality. HBsAg status did not influence viral or immunological responses among the 1679 patients starting HAART. Conclusions: The prevalence of HBV coinfection was 9% in the EuroSIDA cohort. Chronic HBV infection significantly increased liver-related mortality in HIV-1-infected patients but did not impact on progression to AIDS or on viral and immunological responses to HAART.

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HBV, Industrialized countries, HAART

Kumarasamy N, Vallabhaneni S, Flanigan TP, Balakrishnan P, Cecelia A, Carpenter CCJ, Solomon S, Mayer KH. **Rapid viral load suppression following generic highly active antiretroviral therapy in Southern Indian HIV-infected patients.** AIDS 2005;19(6):625-627.

Abstr. We prospectively studied the initial results of 6 months of generic efavirenz-based therapy on the plasma viral load in 40 patients at YRG Centre for AIDS Research and Education, a tertiary HIV referral centre in southern India. The median baseline plasma viral load was 259 000 copies/ml and at 6 months 95% of patients had plasma viral loads less than 400 copies/ml. The data support the use of generic non-nucleoside reverse transcriptase inhibitor-based regimens in resource-limited settings.

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HAART, LICs / Asia, Treatment impact and response

Loko MA, Toure S, Dakoury Dogbo N, Gabillard D, Leroy V, Anglaret X. **Decreasing incidence of pregnancy by decreasing CD4 cell count in HIV-infected women in Cote d'Ivoire: a 7-year cohort study.** AIDS 2005;19(4):443-445.

Abstr. In a cohort study of women of childbearing age in Abidjan, Cote d'Ivoire, we followed 473 HIV-infected women for 1551 person-years, and found that the incidence of pregnancy and livebirth decreased with decreasing CD4 cell counts. This has consequences in terms of scaling-up strategies for highly active antiretroviral therapy (HAART). Women who need HAART will be less likely than those who do not to be recruited into prenatal care facilities.

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LICs / Africa, Obstetrics, Termination of pregnancy / Abortion

Lynen L, Zolfo M, Huyst V, Louis F, Barnardt P, Van de Velde A, De Schacht C, Colebunders R. **Management of Kaposi's sarcoma in resource-limited settings in the era of HAART.** AIDS Reviews 2005;7(1):13-21.

Abstr. The introduction of highly active antiretroviral therapy (HAART) has changed the natural history of AIDS-associated Kaposi's sarcoma (KS). Although the use of HAART remains limited in low-resource settings, there are global initiatives to make these drugs available to several millions of HIV-infected persons. While there are multiple reports of KS regression during HAART with or without chemotherapy, there is little documentation on KS management in resource-limited settings. In this paper we review current KS treatments available worldwide and discuss the implications of the increased access to antiretrovirals for KS treatment strategies in resource-limited settings.

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Clinical manifestations (Others), HAART, LICs

Magoni M, Bassani L, Okong P, Kituuka P, Germinario EP, Giuliano M, Vella S. **Mode of infant feeding and HIV infection in children in a program for prevention of mother-to-child transmission in Uganda.** AIDS 2005;19(4):433-437.

Abstr. Objective: To evaluate the impact of different modalities of infant feeding on HIV transmission in children in a prevention of mother-to-child transmission (PMTCT) program in an urban hospital in Uganda. Methods: HIV-infected pregnant women in the PMTCT program at St Francis Hospital Nsambya, Kampala were offered the chance to participate in the study. Short-course antiretroviral regimens were provided and formula feeding offered free of charge for women choosing not to breastfeed. Mother-infant pairs were followed until 6 months postpartum. HIV status in children was assessed at week 6 and month 6. For the analyses, mother-infant pairs were classified into three groups according to the mode of infant feeding: exclusive formula feeding (EFF), exclusive breastfeeding (EBF) and mixed feeding (MF). Results: A total of 306 children were enrolled. Transmission rates were 8.9% at week 6 (3.4% in the EFF group, 11.2% in the EBF group, 17.1% in the MF group) and 12.0% at month 6 (3.7% in the EFF group, 16.0% in the EBF group, and 20.4% in the MF group). The EBF and MF groups were associated with a significantly higher risk of HIV transmission than the EFF group. No significant risk difference was observed between the EBF and the MF groups. Conclusions: HIV transmission rates were significantly lower in formula-fed infants in comparison with both exclusively breastfed and mixed-fed infants. Transmission through breastfeeding seems to occur mainly in the first weeks after delivery. (c) 2005 Lippincott Williams C Wilkins.

Note: This report is not totally consistent with the conclusions of the ZVITAMBO study in Zimbabwe (see Iliff et al in the same issue). These findings should be interpreted with caution.

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Infant feeding / Breastfeeding, LICs / Africa, MTCT

Mosam A, Cassol E, Page T, Bodasing U, Cassol S, Dawood H, Friedland GH, Scadden DT, Aboobaker J, Jordaan JP, Lalloo UG, Esterhuizen TM, Coovadia HM. **Generic antiretroviral efficacy in AIDS-associated Kaposi's sarcoma in sub-Saharan Africa.** *AIDS* 2005;19(4):441-443.

Abstr. Generic antiretroviral drugs are pivotal in the implementation of WHO's '3 by 5' programme. However, clinical experience with generics in sub-Saharan Africa is insufficiently documented. We report on 50 patients with HIV-associated Kaposi's sarcoma treated with generic fixed-dose highly active antiretroviral therapy. At 52 weeks, 74% achieved an undetectable viral load of < 50 copies/ml, 86% achieved < 400 copies/ml, and a 3.1 log(10) decline from baseline. Side-effects were minimal. The outcomes support the use of generic antiretroviral therapy.

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Clinical manifestations (Others), HAART, LICs / Africa

Nachman S, Gona P, Dankner W, Weinberg A, Yogev R, Gershon A, Rathore M, Read JS, Huang S, Elgie C, Hudgens K, Hughes W. **The rate of serious bacterial infections among HIV-infected children with immune reconstitution who have discontinued opportunistic infection prophylaxis.** *Pediatrics* 2005;115(4):NIL_149-NIL_155.

Abstr. Objective. Receipt of highly active antiretroviral therapy is associated with a decrease in the incidence of opportunistic infections (OIs) among HIV-infected adults. The goal of Pediatric AIDS Clinical Trials Group protocol 1008 was to evaluate prospectively the incidence of serious bacterial infections (SBIs) and other OIs after discontinuation of OI and/or Pneumocystis jirovecii pneumonia (PCP) prophylaxis among HIV-infected pediatric subjects who experienced immune reconstitution while receiving stable antiretroviral therapy. Methods. HIV-infected children and adolescents, 2 to 21 years of age, who had received OI and/or PCP prophylaxis for \geq 6 months were enrolled if they had sustained responses ($>$ 16 weeks before study entry) to antiretroviral therapy, with CD4(+) cell percentages of \geq 20% for patients $>$ 6 years of age or \geq 25% for patients 2 to 6 years of age. Prophylaxis was discontinued at entry. To identify whether any correlation existed between functional immune reconstitution and protection from OIs, subjects were immunized with the hepatitis A virus vaccine. The association between the humoral immune response and the likelihood of developing an OI was evaluated. Results. A total of 235 HIV-infected subjects from 43 participating sites had a median follow-up period of 132 weeks, yielding 547 person-years of observation. Twenty SBIs were observed among 19 subjects, resulting in an incidence rate of 3.66 SBIs per 100 person-years (95% confidence interval: 2.24 - 5.66 SBIs per 100 person-years). Sixteen of the events were presumed bacterial pneumonia, with 4 proven SBIs. One participant experienced 2 separate pneumonia episodes, of presumed bacterial cause. Ten subjects who developed SBIs had baseline CD4(+) cell counts of \geq 750 cells per mm³, and 15 had CD4(+) cell percentages of \geq 25% at the time of their SBIs. Two subjects died as a result of non - SBI-related causes. There were no statistically significant differences in changes over time in CD4(+) cell counts or CD4(+) cell percentages between subjects who experienced primary end points and those who did not. There was no evidence that baseline protease inhibitor use, gender, race/ethnicity, age, or CD4(+) cell count or percentage affected the time to development of a SBI. Conclusions. OI or PCP prophylaxis can be withdrawn safely for HIV-infected pediatric patients who experience CD4(+) cell recovery while receiving stable antiretroviral therapy. More studies are needed to assess the association between antibody responses to neoantigens and the development of SBIs.

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Children, HAART, Industrialized countries, Infections (Others) / Prophylaxis, Treatment complications

Painter TM, Diaby KL, Matia DM, Lin LS, Sibailly TS, Kouassims MK, Ekpini ER, Roels TH, Wiktor SZ. **Sociodemographic factors associated with participation by HIV-1-positive pregnant women in an intervention to prevent mother-to-child transmission of HIV in Cote d'Ivoire.** *International Journal of Std and AIDS* 2005;16(3):237-242.

Abstr. Many HIV-1-seropositive women in Africa who are offered antiretroviral prophylaxis to prevent mother-to-child transmission (MTCT) of HIV do not begin interventions. Research on barriers to participation has not addressed the possible effects of women's sociocultural and economic circumstances. We examined these factors at an MTCT prevention programme in Abidjan, Cote d'Ivoire. We interviewed two groups of women after they had received HIV-positive test results and had been invited by the programme staff to return for monthly follow-up visits before beginning short-course zidovudine prophylaxis. Participants (n = 30) completed follow-up visits and prophylaxis. Non-participants (n = 27) refused or discontinued follow-up visits and did not begin zidovudine. Fewer non-participants had been born in Cote d'Ivoire (67% vs. 97%) or were Ivorian nationals (48% vs. 77%); they had lived in the country for less time (21 vs. 26 median years). They were less likely to be French-literate (37% vs. 77%), and more of them reported having had Koranic education only (18% vs. 0). They more often reported miscarriages, stillbirths, or infant deaths (69% vs. 33%), and had partners with low-ranked jobs (63% vs. 30%). Our findings suggest that the non-participants were more marginal socioculturally and

economically in Ivorian society than participants. Greater attention to mitigating the effects of broader structural factors on women's participation in interventions may increase the effectiveness of MTCT prevention in Africa.

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Adults / Women, LICs / Africa, PMTCT / ARV

Piwoz EG, Iliff PJ, Tavengwa N, Gavin L, Marinda E, Lunney K, Zunguza C, Nathoo KJ, Humphrey JH. **An education and counseling program for preventing breast-feeding-associated HIV transmission in Zimbabwe: Design and impact on maternal knowledge and behavior.** *Journal of Nutrition* 2005;135(4):950-955.

Abstr. International guidance on HIV and infant feeding has evolved over the last decade. In response to these changes, we designed, implemented, and evaluated an education and counseling program for new mothers in Harare, Zimbabwe. The program was implemented within the ZVITAMBO trial, in which 14,110 mother-baby pairs were enrolled within 96 h of delivery and were followed at 6 wk, 3 mo, and 3-mo intervals. Mothers were tested for HIV at delivery but were not required to learn their test results. Infant feeding patterns were determined using data provided up to 3 mo. Formative research was undertaken to guide the design of the program that included group education, individual counseling, videos, and brochures. The program was introduced over a 2-mo period: 11,362, 1311, and 1437 women were enrolled into the trial before, during, and after this period. Exclusive breast-feeding was recommended for mothers of unknown or negative HIV status, and for HIV-positive mothers who chose to breast-feed. A questionnaire assessing HIV knowledge and exposure to the program was administered to 1996 mothers enrolling after the program was initiated. HIV knowledge improved with increasing exposure to the program. Mothers who enrolled when the program was being fully implemented were 70% more likely to learn their HIV status early (< 3 mo) and 8.4 times more likely to exclusively breast-feed than mothers who enrolled before the program began. Formative research aided in the design of a culturally sensitive intervention. The intervention increased relevant knowledge and improved feeding practices among women who primarily did not know their HIV status.

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Infant feeding / Breastfeeding, LICs / Africa, MTCT

Semrau K, Kuhn L, Vwalika C, Kasonde P, Sinkala M, Kankasa C, Shutes E, Aldrovandi G, Thea DA. **Women in couples antenatal HIV counseling and testing are not more likely to report adverse social events.** *AIDS* 2005;19(6):603-609.

Abstr. Background: Couple counseling has been promoted as a strategy to improve uptake of interventions to prevent mother-to-child HIV transmission (pMTCT) and to minimize adverse social outcomes associated with disclosure of HIV status. Objectives: We tested whether women counseled antenatally as part of a couple were more likely to accept HIV testing and nevirapine in a pMTCT program, and whether they would be less likely to experience later adverse social events than women counseled alone. Methods: A pMTCT program that included active community education and outreach to encourage couple counseling and testing was implemented in two antenatal clinics in Lusaka, Zambia. A subset of HIV-positive women was asked to report their experience of adverse social events 6 months after delivery. Couple-counseled women were compared with individual-counseled women stratified by whether or not they had disclosed their HIV status to their partners. Results: Nine percent (868) of 9409 women counseled antenatally were counseled with their husband. Couple-counseled women were more likely to accept HIV testing (96%) than women counseled alone (79%); however uptake of nevirapine was not improved. Six months after delivery, 28% of 324 HIV-positive women reported at least one adverse social event (including physical violence, verbal abuse, divorce or separation). There were no significant differences in reported adverse social events between couple- and individual-counseled women. Conclusions: Couple counseling did not increase the risk of adverse social events associated with HIV disclosure. Support services and interventions to improve social situations for people living with HIV need to be further evaluated. (c) 2005 Lippincott Williams C Wilkins.

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LICs / Africa, VCT

Sungkanuparph S, Kiertiburanakul S, Manosuthi W, Kiatatchasai W, Vibhagool A. **Initiation of highly active antiretroviral therapy in advanced AIDS with CD4 < 50 cells/mm(3) in a resource-limited setting: efficacy and tolerability.** *International Journal of Std and AIDS* 2005;16(3):243-246.

Abstr. In developing countries, patients often present late with advanced AIDS and a very low CD4 cell count. A retrospective cohort study was conducted in HIV-infected patients who had been initiated into highly active antiretroviral therapy (HAART) with CD4 cell count < 50 cells /mm(3). There were 159 patients of mean age 36.6 years and 60.4% had previous major opportunistic infections. Mean CD4 was 22 cells/mm(3) and 80% had

HIV RNA > 100,000copies/mL. The majority of HAART regimens is non-nucleoside reverse transcriptase inhibitor-based (81.8%). In a treated analysis, 50, 71.2, 79.7, 79.4, and 80.1 % of patients achieved undetectable HIV RNA (< 50copies/mL) at 12, 24, 36, 48, and 60 weeks, respectively. The corresponding mean CD4 counts were 95,125, 166, 201, and 225 cells/mm³. Twentytwo patients (13.8%) had adverse drug events and half of these had to discontinue HAART. Initiation of HAART in advanced AIDS with CD4 cell count < 50 cells/mm³ is effective, safe, and well tolerated and should not be delayed.

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HAART, LICs / Asia, Treatment impact and response

Tardieu M, Brunelle F, Raybaud C, Ball W, Barret A, Pautard B, Lachassine E, Mayaux MJ, Blanche S. **Cerebral MR imaging in uninfected children born to HIV-seropositive mothers and perinatally exposed to zidovudine.** American Journal of Neuroradiology 2005;26(4):695-701.

Abstr. BACKGROUND AND PURPOSE: Mitochondrial dysfunction has been reported in HIV-negative children perinatally exposed to zidovudine, a drug often used in HIV-seropositive mothers during pregnancy. The purpose of this study was to determine the incidence of cerebral MR imaging findings in HIV-uninfected children exposed to zidovudine who present with unexplained neurologic symptoms. METHODS: Two expert groups conducted a systematic, retrospective review of all cerebral MR images available in a multicentric, nationwide French prospective cohort of children born to HIV-seropositive mothers to identify imaging abnormalities. Experts were blinded to each others' interpretations, to the children's neurologic symptoms, and to laboratory evidence of mitochondrial dysfunction. The incidence of abnormalities was determined and compared with the neurologic presentation and laboratory evidence of mitochondrial dysfunction. RESULTS: MR images from 49 HIV-uninfected children (mean age, 26 months) were available for study. All children were perinatally exposed to zidovudine. Twenty-two had probable or established mitochondrial dysfunction according to their symptoms and laboratory data. Twenty-seven children without mitochondrial dysfunction presented with unexplained neurologic symptoms (n = 14) or nonneurologic symptoms (n = 7), and six were asymptomatic. Sixteen of 22 MR images in children with mitochondriopathy were considered abnormal in both independent analyses. Diffuse hyperintensity in the supratentorial white matter (n = 9) and in the tegmentum pons (n = 9) were the most frequent anomalies. Imaging abnormalities were often multifocal (n = 10) and sometimes associated with necrotic areas (n = 3) and volume loss (n = 8). Although 19 of 27 MR images of children without mitochondrial dysfunction were mainly normal, abnormal images were observed in five of 14 children with unexplained neurologic symptoms and in three of six asymptomatic children. CONCLUSION. Images observed in children with antiretroviral-induced mitochondrial dysfunction are similar to those observed in congenital mitochondrial diseases. These images were also observed in symptomatic or asymptomatic children without evidence of systemic mitochondrial dysfunction.

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Children, Clinical manifestations (Others), Industrialized countries, PMTCT / ARV

Torres AS, Muniz RM, Madero R, Borque C, Garcia Miguel M, Gomez MID. **Prevalence of fat redistribution and metabolic disorders in human immunodeficiency virus-infected children.** European Journal of Pediatrics 2005;164(5):271-276.

Abstr. In this study we assessed the prevalence of fat redistribution and metabolic disorders in a population of HIV-infected children on antiretroviral treatment. To make associations with epidemiological parameters, clinical-immune status, viral load and highly active antiretroviral therapy (HAART), we performed a cross-sectional study in HIV-infected children. Epidemiological parameters (age, sex, family history), clinical and immune status, viral load, and duration of antiretroviral treatment (ART) and HAART, including protease inhibitors, were recorded. Presence of clinical signs of fat redistribution and lipid, glucose and lactic acid levels were evaluated. A total of 56 HIV-infected children, including 30 boys (54%), aged between 21 months and 18 years (mean 9.5 years) were studied. In all, 49 patients (87.5%) were receiving ART (mean duration 4 years) and 43 (77%) were receiving HAART (mean duration 3.6 years). Fat redistribution or lipodystrophy was present in 14 patients (25%); seven had lipohypertrophy (12.5%), two lipodystrophy (3.5%) and five a mixed pattern (8.9%). Fat redistribution was higher in children older than 11 years (50%). Of the lipodystrophic patients, 71.4% presented hypertriglyceridaemia (> 130 mg/dl) and 57% hypercholesterolaemia (> 180 mg/dl). We found significant associations between lipodystrophy and age, ART and HAART duration and hypertriglyceridaemia (P < 0.001, 0.002, 0.016 and < 0.001, respectively), but no significant association with sex, family history, clinical or immune status and viral load. Conclusion: The prevalence of lipodystrophy was 25% (95% confidence interval 14.8-34.6) with lipohypertrophy being the commonest pattern. Clinical fat redistribution was significantly associated with older age, duration of antiretroviral treatment and highly active antiretroviral therapy and hypertriglyceridaemia.

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Children, HAART, Industrialized countries, Treatment complications

van Leth F, Andrews S, Grinsztejn B, Wilkins E, Lazanas MK, Lange JMA, Montaner J. **The effect of baseline CD4 cell count and HIV-1 viral load on the efficacy and safety of nevirapine or efavirenz-based first-line HAART.** AIDS 2005;19(5):463-471.

Abstr. Background: A substantial number of patients start their first-line antiretroviral therapy at an advanced stage of an HIV-1 infection. Potential differences between specific drug regimens in antiviral efficacy and safety in these patients are of major importance. Methods: A post-hoc analysis within the randomized controlled 2NN trial comparing efficacy between regimes containing nevirapine (NVP), efavirenz (EFV), or both, in addition to stavudine and lamivudine. Primary outcome: risk of virologic failure in different strata of baseline CD4 T-lymphocyte counts and plasma HIV-1 RNA concentrations (pVL). Virologic failure: never reaching a pVL < 400 copies/ml, or a rebound to two consecutive values > 400 copies/ml. Results: The risk of virologic failure was increased at very low CD4 counts (< 25 x 10⁶ cells/l) compared to CD4 counts > 200 x 10⁶ cells/l [hazard ratio (HR), 1.28; 95% confidence interval (CI), 0.93-1.77]. The same was seen for a pVL ≥ 100 000 copies/ml compared to a lower pVL (HR, 1.20; CI, 0.96-1.50). There were no statistically significant differences between NVP and EFV in risk of virologic failure within any of the CD4 or pVL strata, although EFV performed slightly better in the low CD4 stratum. The incidence of rash in the NVP group was significantly higher in female patients with higher CD4 cell counts, while adverse events in the EFV group were not associated with CD4 cell count. Conclusions: Initial antiretroviral therapy including NVP or EFV is effective in patients with an advanced HIV-1 infection. A high baseline CD4 cell count is associated with the occurrence of rash in female patients using NVP.

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Industrialized countries, HAART, Treatment impact and response

Watts H, Lopman B, Nyamukapa C, Gregson S. **Rising incidence and prevalence of orphanhood in Manicaland, Zimbabwe, 1998 to 2003.** AIDS 2005;19(7):717-725.

Abstr. Objective: To quantify and describe orphan incidence in Manicaland, eastern Zimbabwe. Design: Open cohort study. Methods: Statistical analysis of data on 13 740 and 10 308 children, aged 0-14 years, enumerated in household censuses in four socio-economic strata, 1998-2000 and 2001-2003, and 10 184 children seen in both censuses (74% follow-up). Results: Prevalence of all forms of orphanhood increased. The overall rate of losing a parent amongst non-orphans was 2 7.5 per 1000 person-years (py). Paternal orphan incidence (20.2 per 1000 py) was higher than maternal orphan incidence (9.1 per 1000py) and maternal orphans lost their fathers at a faster rate than paternal orphans lost their mothers. Paternal and maternal orphan incidence increased with age. incidence of maternal orphanhood and double orphanhood amongst paternal orphans rose at 20% per annum [incidence rate ratio (IRR) = 1.20; 95% CI, 1.06-1.35] and 71 % per annum (IRR = 1.71; 95% CI, 1.25-2.33), respectively, 1998-2003, but incidence of paternal orphanhood and double orphanhood amongst maternal orphans were unchanged. For 82% of children with a parent who died, the parent was HIV-positive at baseline. More new paternal and double orphans - but not new maternal orphans - than non-orphans had left their baseline household. Mortality was higher in orphans than non-orphans with the highest death rates observed amongst maternal orphans. Conclusions: Orphan incidence and prevalence are high and increasing due to HIV in eastern Zimbabwe. Orphan incidence patterns differ from orphan prevalence patterns and need to be understood if support programmes are to assist children during periods of high vulnerability.

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Children, LICs / Africa

Zaba B, Whitworth J, Marston M, Nakiyingi J, Ruberantwari A, Urassa M, Issingo R, Mwaluko G, Floyd S, Nyondo A, Crampin A. **HIV and mortality of mothers and children - Evidence from cohort studies in Uganda, Tanzania, and Malawi.** Epidemiology 2005;16(3):275-280.

Abstr. Background: The steady decline in child mortality observed in most African countries through the 1960s, 1970s, and 1980s has stalled in many countries in the 1990s because of the AIDS epidemic. However, the census and household survey data that generally are used to produce estimates of child mortality do not permit precise measures of the adverse effect of HIV on child mortality. Methods: To calculate excess risks of child mortality as the result of maternal HIV status, we used pooled data from 3 longitudinal community-based studies that classified births by the mother's HIV status. We also estimated excess risks of child death caused by increased mortality among mothers. The joint effects of maternal HIV status and maternal survival were quantified using multivariate techniques in a survival analysis. Results: Our analysis shows that the excess risk of death

associated with having an HIV-positive mother is 2.9 (95% confidence interval = 2.3-3.6), and this effect lasts throughout childhood. The excess risk associated with a maternal death is 3.9 (2.8-5.5) in the 2-year period centered on the mother's death, with children of both infected and uninfected mothers experiencing higher mortality risks at this time. Conclusion: HIV impacts on child mortality directly through transmission of the virus to newborns by infected mothers and indirectly through higher child mortality rates associated with a maternal death.

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Adults / Women, Children, LICs / Africa, Natural history

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