HIV Care & PMTCT in Resource-Limited Settings

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Back Issues on Line

prepared by the Bordeaux Working Group

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**Abstr.** OBJECTIVE: To describe the characteristics and risk of bacille Calmette-Guerin (BCG) vaccine related disease in human immunodeficiency virus (HIV) infected infants. METHODS: Systematic literature review of articles published from 1950 to April 2009 in the English language. We identified all microbiologically confirmed cases of disseminated BCG disease in vertically HIV-Infected children reported ill the literature. RESULTS: Sixteen observational studies and 11 case reports/series were included. Observational studies suffered from high rates of loss to follow-up and death. Loco-regional BCG disease was reported in both HIV-infected and non-infected children. Disseminated BCG disease was reported only in children with immunodeficiency and only in studies employing sophisticated laboratory techniques. Sixty-nine cases of disseminated BCG were identified in the literature: 47 cases were reported in six observational studies, the majority (41/47) from the Western Cape of South Africa. A Brazilian cohort study reported no cases of disseminated BCG amongst 66 HIV-Infected children observed over a 7-year period. A recent South African surveillance study reported 32 cases of disseminated BCG over a 3-year period, estimating the risk of disseminated BCG to be 992 per 100000 vaccinations in HIV-Infected children. Few cases of severe disseminated TB were reported in the cohort studies among HIV-Infected children vaccinated with BCG. CONCLUSION: Data on the risk of BCG vaccination in HIV-infected children are limited. Targeted surveillance for BCG complications employing sophisticated diagnostic techniques is required to inform vaccination policy.

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**Abstr.** Prevention of mother-to-child transmission (MTCT) of human immunodeficiency virus type 1 (HIV-1) remains a challenge in most resource-limited settings, particularly in Africa. Single-dose and short-course antiretroviral (ARV) regimens are only partially effective and have failed to achieve wide coverage despite their apparent simplicity. More potent ARV combinations are restricted to pregnant women who need treatment for themselves and are also infrequently used. Furthermore, postnatal transmission via breast-feeding is a serious additional threat. Modifications of infant feeding practices aim to reduce HIV1 transmission through breast milk; replacement feeding is neither affordable nor safe for the majority of African women, and early breast-feeding cessation (eg, prior to 6 months of life) requires substantial care and nutritional counseling to be practiced safely. The recent roll out of ARV treatment has changed the paradigm of prevention of MTCT. To date, postnatal ARV interventions that have been evaluated target either maternal ARV treatment to selected breast-feeding women, with good efficacy, or single-drug postexposure prophylaxis for short periods of time to their neonates, with a partial efficacy and at the expense of acquisition of drug-related viral resistance. We hypothesize that a viable solution to eliminate pediatric AIDS lies in the universal provision of fully suppressive ARV regimens to all HIV-1-infected women through pregnancy, delivery, and the entire breast-feeding period. On the basis of available evidence, we suggest translating into practice the recently available evidence on this matter without any further delay.

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Bisson GP, Stringer JSA. **Lost but Not Forgotten-The Economics of Improving Patient Retention in AIDS Treatment Programs - art. no. e1000174.** Plos Medicine 2009;6(10):174-174.

**Notes.** Editorial of Losina paper

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**Free Full Text:** [http://www.plosmedicine.org/article/info%3Adoi%2F10.1371%2Fjournal.pmed.1000174](http://www.plosmedicine.org/article/info%3Adoi%2F10.1371%2Fjournal.pmed.1000174)


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**Abstr.** Background: Nevirapine (NVP) is often prescribed once daily in clinical practice in combination with a once daily nucleoside backbone. We investigated the relationship of NVP dosing with safety and efficacy. Methods: Patients from the Dutch AIDS Therapy Evaluation in the Netherlands (ATHENA) cohort study, Canadian HAART Observational Medical Evaluation and Research (HOMER) cohort and Swiss HIV Cohort Study (SHCS) using NVP-based combination therapy either once daily or twice daily were included. Risk factors for discontinuing NVP because of hypersensitivity reactions (HSRs) were investigated using multivariate logistic regression. Risk factors for virological failure 96 weeks after NVP initiation were identified using logistic regression and Cox models. Results: Of 5,636 patients (774 once daily and 4,862 twice daily), 268 (4.8%) discontinued NVP because of HSR between 2 and 18 weeks. Logistic regression showed that, compared with patients with detectable HIV type-1 (HIV-1) RNA starting twice-daily NVP, there was a significantly higher risk of discontinuation of once-daily NVP because of HSR in patients with detectable HIV-1 RNA at the start of NVP (odds ratio [OR] 1.52; P=0.04), whereas the risk was actually significantly lower in patients starting once-daily NVP with undetectable HIV-1 RNA (OR 0.44; P=0.04). Cox models showed that risk of virological failure was not different for twice- versus once-daily NVP in treatment-naive patients (twice-daily versus once-daily hazard ratio [HR] 1.01; P=0.95), treatment-experienced patients experiencing treatment failure (twice-daily versus once-daily HR 1.22; P=0.30) or patients with undetectable HIV-1 RNA simplifying treatment with NVP (twice-daily versus once-daily HR 1.29; P=0.30). Conclusions: Initiation of a once-daily NVP-based regimen in patients with suppressed viraemia carries a low risk of treatment-limiting HSR. Once- or twice-daily NVP-based regimens appear to have similar antiretroviral efficacy.

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**Abstr. edited.** Background. Responses to antiretroviral therapy (ART) among human immunodeficiency virus (HIV)-infected children in resource-limited settings have recently been reported, but outcomes vary. We sought to derive pooled estimates of the 12-month rate of virologic suppression (HIV RNA, <400 copies/mL) and gain in CD4 cell
percentage (Delta CD4%) for children initiating ART in resource-limited settings. Methods. We conducted a systematic review and meta-analysis of published reports of HIV RNA and CD4 outcomes for treatment-naïve children aged 0-17 years old by means of the Medline, EMBASE (Excerpta Medica Database), and LILACS (Latin American and Caribbean Health Sciences Literature) electronic databases and the Cochrane Clinical Trials Register. Pooled estimates of the reported proportion with HIV RNA <400 copies/mL and Delta CD4% after 12 months of ART were derived using patient-level estimates and fixed-and random-effects models. To approximate intention-to-treat analyses, in sensitivity analyses children with missing 12-month data were assumed to have HIV RNA>400 copies/mL or Delta CD4% of zero. Results. Nine papers reported the proportion of children with HIV RNA <400 copies/mL at 12 months, representing 1457 children initiating ART. 12-month HIV RNA data were available for 1097 children (75%). Twelve studies reported on 12-month CD4% outcomes, representing 5329 children initiating ART. Of these, 2676 were reported to be eligible, and 12-month CD4% data were available for 1839 children. Others were ineligible because they initiated ART <12 mo before data reporting or because only absolute CD4 count was recorded because of age >5 years. In patient-level estimates after 12 months of ART, the pooled proportion with virologic suppression was 70% (95% confidence interval [CI], 67%-73%); the pooled Delta CD4% was 13.7% (95% CI, 11.8%-15.7%). Results from the fixed-and random-effects models were similar. In approximated intention-to-treat analyses, the pooled estimates decreased to 53% with virologic suppression (95% CI, 50%-55%) and to a Delta CD4% of 8.5% (95% CI, 5.5%-11.4%). Conclusions. Pooled estimates of reported virologic and immunologic benefits after 12 months of ART among HIV-infected children in resource-limited settings are comparable with those observed among children in developed settings. Consistency in reporting on reasons for missing data will aid in the evaluation of ART outcomes in resource-limited settings.

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Abstr. Objectives. To assess paediatric antiretroviral treatment (ART) outcomes and their associations from a collaborative cohort representing 20% of the South African national treatment programme. Design and setting. Multi-cohort study of 7 public sector paediatric ART programmes in Gauteng, Western Cape and KwaZulu-Natal provinces. Subjects. ART-naïve children (<= 16 years) who commenced treatment with >3 antiretroviral drugs before March 2008. Outcome measures. Time to death or loss to follow-up were assessed using the Kaplan-Meier method. Associations between baseline characteristics and mortality were assessed with Cox proportional hazards models stratified by site. Immune Status, virological suppression and growth were described in relation to duration of ART. Results. The median (interquartile range) age of 6 078 children with 9 368 child-years of follow-up was 43 (15 - 83) months, with 29% being <18 months. Most were severely ill at ART initiation. More than 75%, of children were appropriately monitored at 6-monthly intervals with viral load suppression (<400 copies/ml) being 80% or above throughout 36 months of treatment. Mortality and retention in care at 3 years were 7.7% (95%, confidence interval 7.0 - 8.6%) and 81.4% (80.1 - 82.6%), respectively. Together with young-age, all markers of disease severity (low weight-for-age z-score, high viral load, severe immune suppression, stage 3/4 disease and anaemia) were independently associated with mortality. Conclusions. Dramatic clinical benefit for children accessing the national ART programme is demonstrated. Higher mortality in infants and those with advanced disease highlights the need for early diagnosis of HIV infection and commencement of ART.

**Abstr.** Background: Despite several years of implementation, prevention of mother-to-child transmission (PMTCT) programmes in many resource poor settings are failing to reach the majority of HIV positive women. We report on a data driven participatory quality improvement intervention implemented in a high HIV prevalence district in South Africa. Methods: A participatory quality improvement intervention was implemented consisting of an initial assessment undertaken by a team of district supervisors, workshops to assess results, identify weaknesses and set improvement targets and continuous monitoring to support changes. Results: The assessment highlighted weaknesses in training and supervision. Routine data revealed poor coverage of all programme indicators except HIV testing. Monthly support to all facilities took place including an orientation to the PMTCT protocol, review of local data and identification of bottlenecks to optimal coverage using a continuous quality improvement approach. One year following the intervention large improvements in programme indicators were observed. Coverage of CD4 testing increased from 40 to 97%, uptake of maternal nevirapine from 57 to 96%, uptake of infant nevirapine from 15 to 68% and six week PCR testing from 24 to 68%. Conclusion: It is estimated that these improvements in coverage could avert 580 new infant infections per year in this district. This relatively simple participatory assessment and intervention process has enabled programme managers to use a data driven approach to improve the coverage of this important programme.

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**Abstr.** BACKGROUND: We aimed to estimate the effect of anti-retroviral therapy (ART) on incident tuberculosis (TB) in a cohort of HIV-infected children. METHODS: We analysed data from ART-naïve, TB disease-free children enrolled between December 2004 and April 2008 into an HIV care program in Kinshasa, Democratic Republic of Congo. To estimate the effect of ART on TB incidence while accounting for time-dependent confounders affected by exposure, a Cox proportional hazards marginal structural model was used. RESULTS: 364 children contributed 596.0 person-years of follow-up. At baseline, the median age was 6.9 years; 163 (44.8%) were in HIV clinical stage 3 or 4. During follow-up, 242 (66.5%) children initiated ART and 81 (22.3%) developed TB. At TB diagnosis, 41 (50.6%) were receiving ART. The TB incidence rate in those receiving ART was 10.2 per 100 person-years [95% confidence interval (CI) 7.4-13.9] compared with 20.4 per 100 person-years (95% CI 14.6-27.8) in those receiving only primary HIV care. TB incidence decreased with time on ART, from 18.9 per 100 person-years in the first 6 months to 5.3 per 100 person-years after 12 months of ART. The model-estimated TB hazard ratio for ART was 0.51 (95% CI 0.27-0.94). CONCLUSIONS: For HIV-infected children in TB-endemic areas, ART reduces the hazard of developing TB by 50%.

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**Abstr.** BACKGROUND: Tobacco smoking is common in human immunodeficiency virus (HIV) infected patients from industrialised countries. In West Africa, few data concerning tobacco consumption exist. METHODS: A cross-sectional survey of the International Epidemiological Database to Evaluate AIDS (IeDEA) network in West Africa was conducted. Health workers administered a questionnaire assessing tobacco and cannabis consumption among patients receiving anti-retroviral treatment. Regular smokers were defined as current smokers who smoked >1 cigarette per day for >= 1 year. RESULTS: Overall, 2920 patients were enrolled in three countries. The prevalence of ever smokers and regular smokers were respectively 46.2% (95%CI 42.8-49.5) and 15.6% (95%CI 13.2-18.0) in men and 3.7% (95%CI 2.9-4.5) and 0.6% (95%CI 0.3-0.9) In women. Regular smoking was associated with being from Cote d'Ivoire or Mali compared to Benin (OR 4.6, 95%CI 2.9-7.3 and 7.7, 95%CI 4.4-13.6), severely impaired immunological status at highly active antiretroviral treatment initiation (OR 1.5, 95%CI 1.1-2.2) and history of tuberculosis (TB; OR 1.8, 95%CI 1.1-3.0). CONCLUSION: There are marked differences in smoking prevalence among these West African countries. This survey approach also provides proof of the association between cigarette smoking and TB in HIV-Infected patients, a major public health issue in this part of the world.

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**Abstr.** Background: Tuberculosis contributes significantly to morbidity and mortality among HIV-infected children in sub-Saharan Africa. Isoniazid prophylaxis can reduce tuberculosis incidence in this population. However, for the treatment to be effective, adherence to the medication must be optimized. We investigated adherence to isoniazid prophylaxis administered daily, compared to three times a week, and predictors of adherence amongst HIV-infected children. Methods: We investigated adherence to study medication in a two centre, randomized trial comparing daily to three times a week dosing of isoniazid. The study was conducted at two tertiary paediatric care centres in Cape Town, South Africa. Over a 5 year period, we followed 324 HIV-infected children aged >= 8 weeks. Adherence information based on pill counts was available for 276 children. Percentage adherence was calculated by counting the number of pills returned. Adherence >= 90% was considered to be optimal. Analysis was done using summary and repeated measures, comparing adherence to the two dosing schedules. Mean percentage adherence (per child during follow-up time) was used to compare the mean of each group as well as the proportion of children achieving an adherence of >= 90% in each group. For repeated measures, percentage adherence (per child per visit) was dichotomized at 90%. A logistic regression model with generalized estimating equations, to account for within-individual correlation, was used to evaluate the impact of the dosing schedule. Adjustments were made for potential confounders and we assessed potential baseline and time-varying adherence determinants. Results: The overall adherence to isoniazid was excellent, with a mean adherence of 94.7% (95% confidence interval [CI] 93.5-95.9); similar mean adherence was achieved by the group taking daily medication (93.8%; 95% CI 92.1-95.6) and by the three times a week group (95.5%; 95% CI 93.8-97.2). Two-hundred and seventeen (78.6%) children achieved a mean adherence of >= 90%. Adherence was similar for daily and three times a week dosing schedules in univariate (odds ratio [OR] 0.88; 95% CI 0.66-1.17; P = 0.38) and multivariate
Children from overcrowded homes were less adherent (adjusted OR 0.71; 95% CI 0.54-0.95; P = 0.02). Age at study visit was predictive of adherence, with better adherence achieved in children older than 4 years (adjusted OR 1.96; 95% CI 1.16-3.32; P = 0.01). Conclusion: Adherence to isoniazid was excellent regardless of the dosing schedule used. Intermittent dosing of isoniazid prophylaxis can be considered as an alternative to daily dosing, without compromising adherence or efficacy.

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Abstr. Objective: To assess technical and operational performance of a dried blood spot (DBS)-based HIV-1 RNA service for remote healthcare facilities in a low-income country. Design: A method comparison and operational evaluation of DBS RNA against conventional tests for early infant diagnosis of HIV and HIV RNA quantitation under field conditions in Tanzania. Methods: DBSs were prepared and plasma was frozen at -80 degrees C. DBSs were mailed and plasma couriered to a central laboratory for testing using the Abbott m2000 system. Infant diagnosis DBSs were also tested for HIV-1 DNA by ROCHE COBAS AmpliPrep/COBAS TaqMan System. Results of DBS RNA were compared with conventional tests; program performance was described. Results: Among 176 infant diagnosis participants, using a threshold of at least 1000 copies/ml, sensitivity and specificity of DBS versus plasma RNA were 1.00 and 0.99, and of DBS RNA versus DBS DNA were 0.97 and 1.00. Among 137 viral load monitoring participants, when plasma and DBS RNA were compared, r value was 0.9709; r value was 0.9675 for at least 5000 copies/ml but was 0.7301 for less than 5000 copies/ml. The highest plasma RNA value at which DBS RNA was not detected was 2084 copies/ml. Median (range) turnaround time from sample collection to result receipt at sites was 23 (4-69) days. The Tanzania mail service successfully transmitted all DBS and results between sites and the central laboratory. Conclusion: Under program conditions in Tanzania, DBS provided HIV-1 RNA results comparable to conventional methods to remote healthcare facilities. DBS RNA testing is an alternative to liquid plasma for HIV-1 RNA services in remote areas.

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Abstr. Background: Data from HIV treatment programs in resource-limited settings show extensive rates of loss to follow-up (LTFU) ranging from 5% to 40% within 6 mo of antiretroviral therapy (ART) initiation. Our objective was to project the clinical impact and cost-effectiveness of interventions to prevent LTFU from HIV care in West Africa. Methods and Findings: We used the Cost-Effectiveness of Preventing AIDS Complications (CEPAC) International model to project the clinical benefits and cost-effectiveness of LTFU-prevention programs from a payer perspective. These programs include components such as eliminating ART co-payments, eliminating charges to patients for opportunistic infection-related drugs, improving personnel training, and providing meals and reimbursing for transportation for participants. The efficacies and costs of these interventions were extensively varied in sensitivity analyses. We used World Health Organization criteria of <3x gross domestic product per capita (3x GDP per capita = US$2,823 for Cote d’Ivoire) as a plausible threshold for "cost-effectiveness." The main results are based on a reported 18% 1-y LTFU rate. With full retention in care, projected per-person discounted life expectancy starting from age 37 y was 144.7 mo (12.1 y). Survival losses from LTFU within 1 y of ART initiation ranged from 73.9 to 80.7 mo. The intervention costing US$22/person/year (e. g., eliminating ART co-payment) would be cost-effective with an efficacy of at least 12%. An intervention costing US$77/person/year (inclusive of all the components described above) would be cost-effective with an efficacy of at least 41%. Conclusions: Interventions that prevent LTFU in resource-limited settings would substantially improve survival and would be cost-effective by international criteria with efficacy of at least 12%-41%, depending on the cost of intervention, based on a reported 18% cumulative incidence of LTFU at 1 y after ART initiation. The commitment to start ART and treat HIV in these settings should include interventions to prevent LTFU.

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Abstr. Objectives: To explore whether private midwives can perform HIV counselling and testing, provide antiretroviral treatment and contraceptives, and how this affects access to services especially among young and HIV-positive women. Methods: A formative study was conducted between January and April 2009 to assess care-seeking practices and perceptions on the prevention of mother-to-child transmission (PMTCT) and family planning services in Wakiso district,! central! Uganda. A household survey supplemented by 12 focus group discussions and 66 key informant interviews was carried out between January and April 2009. Results: 10 706 women, mean age 25.8 years (14-49 years) were interviewed. The majority of women, 4786 (57%) were in the lowest wealth quintile; 62.0% were not using family planning (p<0.000); 56.2% did not access HIV counselling and testing because they feared knowing their HIV status (p<0.013), while 66.5% feared spouses knowing their HIV status (p<0.013). Access to these services among the young women and those with no education was also poor. Private midwives provide HIV testing to 7.8% of their clients; 5.9% received antiretroviral drugs and 8.6% received contraceptives. Client satisfaction with services at private midwifery practices was high. Private midwives are trusted and many clients confide in them. An intervention through private midwives was perceived to improve access because of short distances and no transport costs. Adolescents prioritised confidentiality, while subsidising costs,
community sensitisation and focusing on male spouses were overwhelmingly recommended. Conclusions: Private midwives clinics are potential delivery outlets for PMTCT in Uganda. A well-designed intervention linking them to the public sector and the community could increase access to services.

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**Abstr.** Background: Single-dose nevirapine (sdNVP)-which prevents mother-to-child transmission of HIV-selects non-nucleoside reverse-transcriptase inhibitor (NNRTI) resistance mutations in the majority of women and HIV-infected infants receiving it. This open-label, randomised trial examined the efficacy of short-course zidovudine (AZT) and lamivudine (3TC) with sdNVP in reducing NNRTI resistance in mothers, and as a secondary objective, in infants, in a setting where sdNVP was standard-of-care. Methods and Findings: sdNVP alone, administered at the onset of labour and to the infant, was compared to sdNVP with AZT plus 3TC, given as combivir (CBV) for 4 (NVP/CBV4) or 7 (NVP/CBV7) days, initiated simultaneously with sdNVP in labour; their newborns received the same regimens. Women were randomised 1:1:1. HIV-1 resistance was assessed by population sequencing at: baseline, 2, and 6 wk after birth. An unplanned interim analysis resulted in early stopping of the sdNVP arm. 406 pregnant women were randomised and took study medication (sdNVP 74, NVP/CBV4 164, and NVP/CBV7 168). HIV-1 resistance mutations emerged in 59.2%, 11.7%, and 7.3% of women in the sdNVP, NVP/CBV4, and NVP/CBV7 arms by 6 wk postpartum; differences between NVP-only and both NVP/CBV arms were significant (p<0.0001), but the difference between NVP/CBV4 and NVP/CBV7 was not (p = 0.27). Estimated efficacy comparing combined CBV arms with sdNVP was 85.6%. Similar resistance reductions were seen in infants who were HIV-infected by their 6-wk visit. Conclusions: A short course of AZT plus 3TC, supplementing maternal and infant sdNVP, reduces emergent NNRTI resistance mutations in both mothers and their infants. However, this trial was not powered to detect small differences between the CBV arms.

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**Abstr. edited.** Objective: To compare the response to a nevirapine (NVP)-based highly active antiretroviral therapy (HAART) in HIV-infected Ugandan children, exposed and nonexposed to single-dose NVP (sd NVP) at birth. Methods: HIV-infected study children were initiated on stavudine/lamivudine/NVP as a fixed dose combination. CD4 cell percent and HIV-1 RNA were documented at baseline, 12, 24, 36, and 48 weeks post-initiation of HAART. Results: Ninety-two children were enrolled in the study, 44 in the sd NVP-exposed and 48 in the nonexposed cohort. The median age at enrollment was 1.7 years [interquartile range (IQR) 1.2-2.4] and 7.8 years (IQR 5.9-9.2) in the sd NVP-exposed and nonexposed cohorts, respectively (P < 0.001). At baseline and week 48
post-HAART, the median CD4 cell percentages were 14% and 33% for the NVP-exposed group and 8% and 22.5% in the nonexposed group (P < 0.0001). The median (IQR) viral load at baseline was 650,568 (359,979-2,086,613) RNA copies/mL and 239,027 (105,904-494,813) RNA copies/mL in the NVP-exposed and nonexposed cohorts, respectively. After 48 weeks of HAART, 76% of the NVP-exposed and 80% of the nonexposed children had a median viral load of <400 copies/mL (P = 0.74). In multivariate analysis, none of the baseline factors including sd-NVP exposure, viral load, CD4 percent, age, height-for-age z-score (HAZ), and weight-for-age z-score (WAZ), sex, and WHO stage had an effect on the outcome of virologic treatment success. There were 2 deaths during the 48-week study follow-up [in the nonexposed group] but they were not related to study ART. One child who was severely immunosuppressed at baseline (CD4 cell count 0.5%) and died 2 weeks after enrollment from severe pneumonia and the other death at 44 weeks was due to HIV nephropathy. Conclusions: Both HIV-infected Ugandan older infants and children that were exposed and not exposed to sd NVP at birth had favorable treatment outcomes on NVP-containing HAART.

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Abstr. Objective: To assess the 9-month HIV-free survival of children with two strategies to prevent HIV mother-to-child transmission. Design: Nonrandomized interventional cohort study. Setting: Four public health centres in Rwanda. Participants: Between May 2005 and January 2007, all consenting HIV-infected pregnant women were included. Intervention: Women could choose the mode of feeding for their infant: breastfeeding with maternal HAART for 6 months or formula feeding. All received HAART from 28 weeks of gestation. Nine-month cumulative probabilities of HIV transmission and HIV-free survival were determined using the Kaplan-Meier method and compared using the log-rank test. Determinants were analysed using a Cox model analysis. Results: Of the 532 first-liveborn infants, 227 (43.7%) were breastfeeding and 305 (57.3%) were formula feeding. Overall, seven (1.3%) children were HIV-infected of whom six were infected in utero. Only one child in the breastfeeding group became infected between months 3 and 7, corresponding to a 9-month Cumulative risk of postnatal infection of 0.5% [95% confidence interval (CI) 0.1-3.4%; P = 0.24] with breastfeeding. Nine-month cumulative mortality was 3.3% (95% CI 1.6-6.9%) in the breastfeeding arm group and 5.7% (95% CI 3.6-9.21%) for the formula feeding group (P = 0.20). HIV-free survival by 9 months was 95% (95% CI 91-97%) in the breastfeeding group and 94% (95% CI 91-96%) for the formula feeding group (P = 0.66), with no significant difference in the adjusted analysis (adjusted hazard ratio for breastfeeding: 1.2 [95% CI 0.5-2.9%]). Conclusion: Maternal HAART while breastfeeding could be a promising alternative strategy in resource-limited countries.

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Abstr. BACKGROUND The use of fixed-dose combination nucleoside reverse-transcriptase inhibitors (NRTIs) with a nonnucleoside reverse-transcriptase inhibitor or a ritonavir-boosted protease inhibitor is recommended as initial therapy in patients with human immunodeficiency virus type 1 (HIV-1) infection, but which NRTI combination has greater efficacy and safety is not known. METHODS In a randomized, blinded equivalence study involving 1858 eligible patients, we compared four once-daily anti-retroviral regimens as initial therapy for HIV-1 infection: abacavir-lamivudine or tenofovir disoproxil fumarate (DF)-emtricitabine plus efavirenz or ritonavir-boosted atazanavir. The primary efficacy end point was the time from randomization to virologic failure (defined as a confirmed HIV-1 RNA level >= 1000 copies per milliliter at or after 16 weeks and before 24 weeks, or = 200 copies per milliliter at or after 24 weeks). RESULTS A scheduled interim review by an independent data and safety monitoring board showed significant differences in virologic efficacy, according to the NRTI combination, among patients with screening HIV-1 RNA levels of 100,000 copies per milliliter or more. At a median follow-up of 60 weeks, among the 797 patients with screening HIV-1 RNA levels of 100,000 copies per milliliter or more, the time to virologic failure was significantly shorter in the abacavir-lamivudine group than in the tenofovir DF-emtricitabine group (hazard ratio, 2.33; 95% confidence interval, 1.46 to 3.72; P<0.001), with 57 virologic failures (14%) in the abacavir-lamivudine group versus 26 (7%) in the tenofovir DF-emtricitabine group. The time to the first adverse event was also shorter in the abacavir-lamivudine group (P<0.001). There was no significant difference between the study groups in the change from the baseline CD4 cell count at week 48. CONCLUSIONS In patients with screening HIV-1 RNA levels of 100,000 copies per milliliter or more, the times to virologic failure and the first adverse event were both significantly shorter in patients randomly assigned to abacavir-lamivudine than in those assigned to tenofovir DF-emtricitabine. (ClinicalTrials.gov number, NCT00118898.).

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Abstr. Background: The shortage of human resources for health, and in particular physicians, is one of the major barriers to achieve universal access to HIV care and treatment. In September 2005, a pilot program of nurse-centered antiretroviral treatment (ART) prescription was launched in three rural primary health centers in Rwanda. We retrospectively evaluated the feasibility and effectiveness of this task-shifting model using descriptive data. Methods and Findings: Medical records of 1,076 patients enrolled in HIV care and treatment services from September 2005 to March 2008 were reviewed to assess: (i) compliance with national guidelines for ART eligibility and prescription, and patient monitoring and (ii) key outcomes, such as retention, body weight, and CD4 cell count change at 6, 12, 18, and 24 mo after ART initiation. Of these, no ineligible patients were started on ART and only one patient received an inappropriate ART prescription. Of the 435 patients who initiated ART, the vast majority had adherence and side effects assessed at each clinic visit (89% and 84%, respectively). By March 2008, 390 (90%) patients were alive on ART, 29 (7%) had died, one (<1%) was lost to
follow-up, and none had stopped treatment. Patient retention was about 92% by 12 mo and 91% by 24 mo. Depending on initial stage of disease, mean CD4 cell count increased between 97 and 128 cells/μl in the first 6 mo after treatment initiation and between 79 and 129 cells/μl from 6 to 24 mo of treatment. Mean weight increased significantly in the first 6 mo, between 1.8 and 4.3 kg, with no significant increases from 6 to 24 mo.

Conclusions: Patient outcomes in our pilot program compared favorably with other ART cohorts in sub-Saharan Africa and with those from a recent evaluation of the national ART program in Rwanda. These findings suggest that nurses can effectively and safely prescribe ART when given adequate training, mentoring, and support.

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Selections of the text. Women of reproductive age are disproportionately affected by the HIV/AIDS epidemic, especially in sub-Saharan Africa where women account for nearly 60% of people living with HIV. Consequently, the family planning and HIV fields intersect in a number of crucial ways: (1) Many women are simultaneously at risk for both unintended pregnancy and HIV infection. Countries with the greatest burden of HIV also have high levels of unmet need for family planning; (2) Like all women, HIV-positive women have a right to make reproductive decisions free of coercion; (3) For women with HIV who want to become pregnant, use of antiretroviral prophylaxis during pregnancy can reduce mother-to-child transmission of HIV. Afterwards, family planning services that promote healthy timing and spacing of pregnancies are important to reduce the risk of adverse pregnancy outcomes such as low birth weight, preterm birth and infant mortality; (4) For women with HIV who do not wish to become pregnant, family planning is a proven, cost-effective strategy for preventing mother-to-child transmission of HIV (PMTCT) and, therefore, reducing the number of children needing HIV treatment, care and support; (5) Barrier methods of contraception – namely, male and female condoms – can protect against both unintended pregnancy and sexual transmission of HIV; (6) HIV services provide an opportunity to reach women and men at risk of, and living with, HIV with family planning information and services; (7) Family planning services, particularly in generalized epidemics, provide an opportunity to increase access to HIV counseling and testing, and other HIV services.

However, rather than being natural allies, family planning and HIV have remained strange bedfellows. Rates of unintended pregnancies remain alarmingly high in women with HIV, and family planning interventions have been underutilized in HIV prevention, care and treatment programs. In addition, HIV programs have emerged primarily as separate ‘silos’ and only minimal efforts have been made to leverage and integrate them with existing family planning infrastructures.

This supplement originated from the belief that more evidence is needed to compel funders, policymakers, program planners and implementers to act on the synergies between the two fields and enhance the public health impact of reproductive health and HIV programs. The contents of this supplement represent research being conducted within three broad areas: behavioral research examining contraceptive practices and fertility desires of HIV-positive women and couples; biomedical research addressing the
safety and effectiveness of contraceptive methods for HIV-positive women; and programmatic research evaluating service delivery approaches to integrating family planning and HIV services. Taken together, the studies published in this supplement expand the evidence base regarding how the family planning and HIV fields are related and how they can be better integrated in practice.

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**Abstr.** Objective The aim of the study was to examine the rates and predictors of treatment modification following combination antiretroviral therapy (cART) failure in Asian patients with HIV enrolled in the TREAT Asia HIV Observational Database (TAHOD). Methods Treatment failure (immunological, virological and clinical) was defined by World Health Organization criteria. Countries were categorized as high or low income by World Bank criteria. Results Among 2446 patients who initiated cART, 447 were documented to have developed treatment failure over 5697 person-years (7.8 per 100 person-years). A total of 253 patients changed at least one drug after failure (51.6 per 100 person-years). There was no difference between patients from high- and low-income countries [adjusted hazard ratio (HR) 1.02; P=0.891]. Advanced disease stage [Centers for Disease Control and Prevention (CDC) category C vs. A; adjusted HR 1.38, P=0.040], a lower CD4 count (>= 51 cells/μL vs. < 50 cells/μL; adjusted HR 0.61, P=0.022) and a higher HIV viral load (>= 400 HIV-1 RNA copies/mL vs. < 400 copies/mL; adjusted HR 2.69, P < 0.001) were associated with a higher rate of treatment modification after failure. Compared with patients from low-income countries, patients from high-income countries were more likely to change two or more drugs (67% vs. 49%; P=0.009) and to change to a protease-inhibitor-containing regimen (48% vs. 16%; P < 0.001). Conclusions In a cohort of Asian patients with HIV infection, nearly half remained on the failing regimen in the first year following documented treatment failure. This deferred modification is likely to have negative implications for accumulation of drug resistance and response to second-line treatment. There is a need to scale up the availability of second-line regimens and virological monitoring in this region.

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