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.** Background: In many HIV programmes in Africa, patients are assessed clinically and prepared for antiretroviral treatment over a period of 4-12 weeks. Mortality rates following initiation of ART are very high largely because patients present late with advanced disease. The rates of mortality and retention during the pre-treatment period are not well understood. We conducted an observational study to determine these rates. Methods: HIV-infected subjects presenting at The AIDS Support Clinic in Jinja, SE Uganda, were assessed for antiretroviral therapy (ART). Eligible subjects were given information and counselling in 3 visits done over 4-6 weeks in preparation for treatment. Those who did not complete screening were followed-up at home. Survival analysis was done using poisson regression. Results: 4321 HIV-infected subjects were screened of whom 2483 were eligible for ART on clinical or immunological grounds. Of these, 637 (26%) did not complete screening and did not start ART. Male sex and low CD4 count were associated independently with not completing screening. At follow-up at a median 351 days, 181 (28%) had died, 189 (30%) reported that they were on ART with a different provider, 158 (25%) were alive but said they were not on ART and 109 (17%) were lost to follow-up. Death rates (95% CI) per 100 person-years were 34 (22, 55) (n. 18) within one month and 37 (29, 48) (n. 33) within 3 months. 70/158 (44%) subjects seen at follow-up said they had not started ART because they could not afford transport. Conclusion: About a quarter of subjects eligible for ART did not complete screening and pretreatment mortality was very high even though patients in this setting were well informed. For many families, the high cost of transport is a major barrier preventing access to ART.

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**Abstr.** Background: Current World Health Organization (WHO) guidelines for treatment of HIV in resource-limited settings call for 2 antiretroviral regimens. The effectiveness and cost-effectiveness of increasing the number of antiretroviral regimens is unknown. Methods: Using a simulation model, we compared the survival and costs of current WHO regimens with two 3-regimen strategies: an initial regimen of 3 nucleoside reverse transcriptase inhibitors followed by the WHO regimens and the WHO regimens followed by a regimen with a second-generation boosted protease inhibitor (2bPI). We evaluated monitoring with CD4 counts only and with both CD4 counts and viral load. We used cost and effectiveness data from Cape Town and tested all assumptions in sensitivity analyses. Results: Over the lifetime of the cohort, 25.6% of individuals failed both WHO regimens by virologic criteria. However, when patients were monitored using CD4 counts alone, only 6.5% were prescribed additional highly active antiretroviral therapy due to missed and delayed detection of failure. The life expectancy gain for individuals who took a 2bPI was 6.7-8.9 months, depending on the monitoring strategy. When CD4 alone was available, adding a regimen with a 2bPI was associated with an incremental cost-effectiveness ratio of $2581 per year of life gained, and when viral load was available, the ratio was $6519 per year of life gained. Strategies with triple-nucleoside reverse transcriptase inhibitor regimens in initial therapy were dominated. Results were sensitive to the price of 2bPIs. Conclusions: About 1 in 4 individuals who start highly active antiretroviral therapy in sub-Saharan Africa will fail currently recommended regimens. At
current prices, adding a regimen with a 2bPI is cost effective for South Africa and other middle-income countries by WHO standards.

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**Abstr.** BACKGROUND: Human immunodeficiency virus (HIV)-infected patients are at higher risk of malignancies. In addition to traditional determinants, a specific deleterious effect of HIV and immunodeficiency is speculated. We aimed at studying the association between immunological and virological characteristics of HIV-infected patients in care and the risk of acquired immunodeficiency syndrome (AIDS)-defining and non-AIDS-defining malignancies. METHODS: Patients consecutively enrolled in the hospital-based Agence Nationale de Recherche sur le Sida (ANRS) CO3 Aquitaine Cohort were included if the duration of follow-up was >3 months during the period 1998-2006. Multivariate modeling used an extended Cox proportional hazards model for time-dependent covariates and delayed entry. RESULTS: The 4194 patients included in the study developed 251 first malignancies during 22,389 person-years. A higher incidence of AIDS-defining malignancies (107 cases) was independently associated with (1) both longer and current exposures to a plasma HIV RNA level >500 copies/mL (hazard ratio [HR], 1.27 per year [P<.001] and 3.30 [P<.001], respectively) and (2) both longer and current exposure to a CD4(+) cell count <200 cells/mm(3) (HR, 1.36 per year [P<.001] and 6.33 [P<.001], respectively). A higher incidence of non-AIDS-defining malignancies (144 cases) was independently associated with longer and current exposure to a CD4(+) cell count <500 cells/mm(3) (HR, 1.13 per year [P=.01] and 2.07 [P<.001], respectively) and male sex (HR, 1.69; P=.02) but not with plasma HIV RNA level (P=.49 and P=.10 for cumulative and current exposures, respectively). CONCLUSIONS: Uncontrolled plasma HIV RNA level was independently associated with a higher likelihood of developing AIDS-defining malignancies, whereas immunosuppression was associated with a higher risk of developing any type of malignancies. Antiretroviral treatment should aim at reaching and maintaining a CD4(+) count >500 cells/mm(3) to prevent the occurrence of malignancy, this should be integrated to malignancy-prevention policies.

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**Abstr.** Background. Although many studies have reported high early mortality among patients enrolled in antiretroviral therapy (ART) programs in sub-Saharan Africa—particularly among those individuals with advanced immunodeficiency—few studies have reported the most common causes of these early deaths. Methods. We determined cause-specific mortality and the contribution of immune reconstitution inflammatory syndrome (IRIS) in a well-characterized patient cohort in Kampala, Uganda, over a 36-month period of ART. Results. In a cohort of patients who initiated antiretroviral therapy in Uganda, we observed a high early mortality rate among patients with advanced disease. The most common causes of death were tuberculosis and cryptococcal meningitis. The contribution of immune reconstitution inflammatory syndrome to mortality was limited.
Conclusions. We show a significant early mortality in our ART cohort in resource-limited settings that is driven by advanced human immunodeficiency virus disease and characterized by low CD4 cell counts. In our experience, the contribution of IRIS to this observed early mortality is limited.

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Abstr. South Africa is one of only 12 countries in which mortality rates for children have increased since the baseline for the Millennium Development Goals (MDGs) in 1990. Continuing poverty and the HIV/AIDS epidemic are important factors. Additionally, suboptimum implementation of high-impact interventions limits programme effectiveness; between a quarter and half of maternal, neonatal, and child deaths in national audits have an avoidable health-system factor contributing to the death. Using the LiST model, we estimate that 11500 infants' lives could be saved by effective implementation of basic neonatal care at 95% coverage. Similar coverage of dual-therapy prevention of mother-to-child transmission with appropriate feeding choices could save 37 200 children's lives in South Africa per year in 2015 compared with 2008. These interventions would also avert many maternal deaths and stillbirths. The total cost of such a target package is US$1.5 billion per year, 24% of the public-sector health expenditure; the incremental cost is $220 million per year. Such progress would put South Africa squarely on track to meet MDG 4 and probably also MDG 5. The costs are affordable and the key gap is leadership and effective implementation at every level of the health system, including national and local accountability for-service provision.

Notes. Part of The Lancet special issue on Health in South Africa [2009;374(9692)].

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Abstr. Sub-Saharan Africa is the epicentre of the HIV pandemic but there are few reports of HIV-related kidney diseases in children in this region. This study aimed to determine the prevalence of proteinuria in HIV-infected children at the Lagos University Teaching Hospital. Proteinuria was determined using urine protein-creatinine ratio. CD4+ cell count was determined for all the HIV-infected children. The mean age of the HIV-infected children was 74.4 +/- 35.6 months with a male: female ratio of 3:2. Compared with 6% of the 50 controls 20.5% of the 88 HIV-infected children had proteinuria (p = 0.026). Of 20 children with advanced clinical stage 40% had proteinuria compared with 14.7% of 68 children with milder stage (p = 0.004). Similarly, proteinuria was commoner among those with severe immunosuppression (p = 0.014). HAART use was not associated with significant difference in proteinuria prevalence (p = 0.491). Proteinuria was frequent among HIV-infected children, especially among those with advanced disease.

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**Abstr.** Background: Dried spots on filter paper made of whole blood (dried blood spots; DBS), plasma (dried plasma spots; DPS) or serum (dried serum spots) hold promise as an affordable and practical alternative specimen source to liquid plasma for HIV type-1 (HIV-1) viral load determination and drug resistance genotyping in the context of the rapidly expanding access to antiretroviral therapy (ART) for HIV-1-infected individuals in low- and middle-income countries. This report reviews the current evidence for their utility. Methods: We systematically searched the English language literature published before 2009 on Medline, the websites of the World Health Organization and US Centers for Disease Control and Prevention, abstracts presented at relevant international conferences and references from relevant articles. Results: Data indicate that HIV-1 viral load determination and resistance genotyping from DBS and DPS is feasible, yielding comparable test performances, even after storage. Limitations include reduced analytical sensitivity resulting from small analyte volumes (approximately 3.5 log(10) copies/ml at 50 μl sample volume), nucleic acid degradation under extreme environmental conditions, impaired efficiency of nucleic acid extraction, potential interference of archived proviral DNA in genotypes obtained from DBS and the excision of spots from the filters in high-volume testing. Conclusions: This technology offers the advantages of a stable specimen matrix, ease of sample collection and shipment. The current sensitivity in drug resistance testing is appropriate for public health surveillance among pretreatment populations. However, consistently improved analytical sensitivity is needed for their routine application in the therapeutic monitoring of individuals receiving ART, particularly at the onset of treatment failure.

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Hoffmann CJ, Charalambous S, Fielding KL, Innes C, Chaisson RE, Grant AD, Churchyard GJ. HIV suppression with stavudine 30 mg versus 40 mg in adults over 60 kg on antiretroviral therapy in South Africa. AIDS 2009;23(13):1784-1786.

**Abstr.** In 2007, the WHO recommended a maximum stavudine dose of 30 mg. We compared virologic suppression among patients weighing more than 60 kg and receiving stavudine 30 mg (n = 110) versus 40 mg (n = 508) in community HIV clinics in South Africa, before and after guidelines changed. At 6 months, HIV RNA less than 400 copies/ml was achieved in 79% and 81% receiving 30 and 40 mg stavudine, respectively (chi(2), P = 0.6). In regression modeling, including baseline HIV RNA and non-nucleoside reverse transcriptase inhibitor agent, stavudine dose remained unassociated with suppression.

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**Abstr.** Background. Monitoring of antiretroviral treatment (ART) with human immunodeficiency virus (HIV) viral loads, as recommended in industrialized countries, is rarely available in resource-limited settings because of the high costs and stringent requirements for storage and transport of plasma. Dried blood spots (DBS) can be an alternative to plasma, but the use of DBS has not been assessed under field conditions in
rural Africa. The present study investigates the performance of DBS in HIV viral load monitoring of patients who received ART in rural Tanzania. Patients and Methods. From November 2007 through June 2008, parallel plasma and DBS specimens were obtained from patients who received ART at Haydom Lutheran Hospital in rural Tanzania. DBS specimens were stored at tropical room temperature for 3 weeks before testing with the NucliSENS EasyQ HIV-1 v1.2 assay. Results obtained with DBS were compared with results obtained with use of a gold-standard plasma assay. Results. Ninety-eight plasma-DBS pairs were compared, and plasma viral loads ranged from <40 to >1,000,000 copies/mL. The correlation between plasma and DBS viral load was strong (R² = 0.75). The mean difference (+/- standard deviation) was log 10 copies/mL, and only 8 samples showed >1 log(10) copies/mL difference. 0.04 +/- 0.57 HIV type 1 RNA was detected in 7%, 60%, and 100% of DBS specimens with corresponding plasma viral loads of 40-999, 1000-2999, and >= 3000 copies/mL, respectively. Conclusions. DBS, in combination with the NucliSENS EasyQ HIV-1 v1.2 assay, performed well in monitoring HIV viral loads in patients who received ART in rural Tanzania, although the sensitivity was reduced when viral burden was low. The use of DBS can simplify virological monitoring in resource-limited settings.

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Abstr. Background: Increased funding for global human immunodeficiency virus prevention and control in developing countries has created both a challenge and an opportunity for achieving long-term global health goals. This paper describes a programme in Zimbabwe aimed at responding more effectively to the HIV/AIDS epidemic by reinforcing a critical competence-based training institution and producing public health leaders. Methods: The programme used new HIV/AIDS programme-specific funds to build on the assets of a local education institution to strengthen and expand the general public health leadership capacity in Zimbabwe, simultaneously ensuring that they were trained in HIV interventions. Results: The programme increased both numbers of graduates and retention of faculty. The expanded HIV/AIDS curriculum was associated with a substantial increase in trainee projects related to HIV. The increased number of public health professionals has led to a number of practically trained persons working in public health leadership positions in the ministry, including in HIV/AIDS programmes. Conclusion: Investment of a modest proportion of new HIV/AIDS resources in targeted public health leadership training programmes can assist in building capacity to lead and manage national HIV and other public health programmes.

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Abstr. OBJECTIVES To examine the accuracy of the World Health Organization immunological criteria for virological failure of antiretroviral treatment. METHODS Analysis of 10 treatment programmes in Africa and South America that monitor both CD4 cell counts and HIV-1 viral load. Adult patients with at least two CD4 counts and viral load measurements between month 6 and 18 after starting a non-nucleoside reverse transcriptase inhibitor-based regimen were included. WHO immunological criteria include
CD4 counts persistently < 100 cells/μL, a fall below the baseline CD4 count, or a fall of > 50% from the peak value. Virological failure was defined as two measurements ≥ 100 000 copies/ml (higher threshold) or ≥ 500 copies/ml (lower threshold). Measures of accuracy with exact binomial 95% confidence intervals (CI) were calculated. RESULTS A total of 2009 patients were included. During 1856 person-years of follow up 63 patients met the immunological criteria and 35 patients (higher threshold) and 95 patients (lower threshold) met the virological criteria. Sensitivity [95% confidence interval (CI)] was 17.1% (6.6-33.6%) for the higher and 12.6% (6.7-21.0%) for the lower threshold. Corresponding results for specificity were 97.1% (96.3-97.8%) and 97.3% (96.5-98.0%), for positive predictive value 9.5% (3.6-19.6%) and 19.0% (10.2-30.9%) and for negative predictive value 98.5% (97.9-99.0%) and 95.7% (94.7-96.6%). CONCLUSIONS The positive predictive value of the WHO immunological criteria for virological failure of antiretroviral treatment in resource-limited settings is poor, but the negative predictive value is high. Immunological criteria are more appropriate for ruling out than for ruling in virological failure in resource-limited settings.

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Abstr. Background Use of raltegravir with optimum background therapy is effective and well tolerated in treatment-experienced patients with multidrug-resistant HIV-1 infection. We compared the safety and efficacy of raltegravir with efavirenz as part of combination antiretroviral therapy for treatment-naive patients. Methods Patients from 67 study centres on five continents were enrolled between Sept 14, 2006, and June 5, 2008. Eligible patients were infected with HIV-1, had viral RNA (vRNA) concentration of more than 5000 copies per mL, and no baseline resistance to efavirenz, tenofovir, or emtricitabine. Patients were randomly allocated by interactive voice response system in a 1:1 ratio (double-blind) to receive 400 mg oral raltegravir twice daily or 600 mg oral efavirenz once daily, in combination with tenofovir and emtricitabine. The primary efficacy endpoint was achievement of a vRNA concentration of less than 50 copies per mL at week 48. The primary analysis was per protocol. The margin of non-inferiority was 12%. This study is registered with ClinicalTrials.gov, number NCT00369941. Findings 566 patients were enrolled and randomly allocated to treatment, of whom 281 received raltegravir, 282 received efavirenz, and three were never treated. At baseline, 297 (53%) patients had more than 100 000 vRNA copies per mL and 267 (47%) had CD4 counts of 200 cells per μL or less. The main analysis (with non-completion counted as failure) showed that 86.1% (n=241 patients) of the raltegravir group and 81.9% (n=230) of the efavirenz group achieved the primary endpoint (difference 4.2%, 95% CI -1.9 to 10.3). The time to achieve such viral suppression was shorter for patients on raltegravir than on efavirenz (log-rank test p<0.0001). Significantly fewer drug-related clinical adverse events occurred in patients on raltegravir (n=124 [44.1%]) than those on efavirenz (n=217 [77.0%]; difference -32.8%, 95% CI -40.2 to -25.0, p<0.0001). Serious drug-related clinical adverse events occurred in less than 2% of patients in each drug group. Interpretation Raltegravir-based combination treatment had rapid and potent antiretroviral activity, which was non-inferior to that of efavirenz at week 48. Raltegravir is a well tolerated alternative to efavirenz as part of a combination regimen against HIV-1 in treatment-naive patients.

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Abstr. Background: By December 2007, over 48,000 persons had initiated antiretroviral treatment (ART) at 171 clinics in Rwanda. Assessing national ART program outcomes is essential to determine whether programs have the desired impact. Methods: We conducted a retrospective cohort study to assess key 6- and 12-month outcomes among a nationally representative, stratified, random sample of 3194 adults (>= 15 years) who initiated ART from January 1, 2004, through December 31, 2005. Findings: At ART initiation, the median patient age was 37 years and 65% were female. Overall, the baseline median CD4(+) cell count was 141 cells per microliter. At 6 and 12 months after ART initiation, 92% and 86% of patients, respectively, remained on ART at their original site. By 6 months, 3.6% were dead and 3.4% were lost to follow-up; by 12 months, 4.6%, were dead and 4.9% were lost to follow-up. Among patients with available follow-up CD4(+) cell count data, median CD4(+) cell counts increased by 98 cells per microliter and 9 cells per microliter at 6 and 12 months after ART initiation, respectively. Conclusions: Rwanda's national ART program achieved excellent 6- and 12-month retention and immunologic outcomes during the first 2 years of rapid scale-up. Routine supervision is required to improve compliance with clinical guidelines and data quality.

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Abstr. Background: Safety and effectiveness of efficacious antiretroviral (ARV) regimens beyond single-dose nevirapine (sdNVP) for prevention of mother-to-child transmission (PMTCT) have been demonstrated in well-controlled clinical studies or in secondary-and tertiary-level facilities in developing countries. This paper reports on implementation of and factors associated with efficacious ARV regimens among HIV-positive pregnant women attending antenatal clinics in primary health centers (PHCs) in Zambia. Methods: Blood sample taken for CD4 cell count, availability of CD4 count results, type of ARV prophylaxis for mothers, and additional PMTCT service data were collected for HIV-positive pregnant women and newborns who attended 60 PHCs between April 2007 and March 2008. Results: Of 14,815 HIV-positive pregnant women registered in the 60 PHCs, 2,528 (17.1%) had their CD4 cells counted; of those, 1,680 (66.5%) had CD4 count <= 350 cells/mm(3) and thus were eligible for combination antiretroviral treatment (cART); and of those, 581 (73.0%) were initiated on cART. The proportion of HIV-positive pregnant women whose blood sample was collected for CD4 cell count was positively associated with (1) blood-draw for CD4 count occurring on the same day as determination of HIV-positive status; (2) CD4 results sent back to the health facilities within seven days; (3) facilities without providers trained to offer ART; and (4) urban location of PHC. Initiation of cART among HIV-positive pregnant women was associated with the PHC's capacity to provide care and antiretroviral treatment services. Overall, of the 14,815 HIV-positive pregnant women registered, 10,015 were initiated on any type of ARV regimen: 581 on cART, 3,041 on short course double ARV regimen, and 6,393 on sdNVP. Conclusion: Efficacious ARV regimens beyond sdNVP can be implemented in resource-constrained PHCs. The majority (73.0%) of women identified eligible for ART were initiated on cART; however, a minority

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(11.3%) of HIV-positive pregnant women were assessed for CD4 count and had their test results available. Factors associated with implementation of more efficacious ARV regimens include timing of blood-draw for CD4 count and capacity to initiate cART onsite where PMTCT services were being offered.

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**Abstr.** Background. Vitamin D is a strong immunomodulator and may protect against adverse pregnancy outcomes, mother-to-child transmission (MTCT) of human immunodeficiency virus (HIV), and child mortality. Methods. A total of 884 HIV-infected pregnant women who were participating in a vitamin supplementation trial in Tanzania were monitored to assess pregnancy outcomes and child mortality. The association of these outcomes with maternal vitamin D status at enrollment was examined in an observational analysis. Results. No association was observed between maternal vitamin D status and adverse pregnancy outcomes, including low birth weight and preterm birth. In multivariate models, a low maternal vitamin D level (< 32 ng/mL) was associated with a 50% higher risk (95% confidence interval [CI], 2%-120%) of MTCT of HIV at 6 weeks, a 2-fold higher risk of MTCT of HIV through breast-feeding among children who were HIV uninfected at 6 weeks (95% CI, 1.08-3.82), and a 46% higher overall risk of HIV infection (95% CI, 11%-91%). Children born to women with a low vitamin D level had a 61% higher risk of dying during follow-up (95% CI, 25%-107%). Conclusions. If found to be efficacious in randomized trials, vitamin D supplementation could prove to be an inexpensive method of reducing the burden of HIV infection and death among children, particularly in resource-limited settings.

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**Abstr.** Background: Infants born to HIV-infected women should receive HIV testing to allow early diagnosis and treatment. Recommendations for resource-limited settings stress laboratory-based virologic assays. While effective, these tests are logistically complex and expensive. This study explored the cost-effectiveness of incorporating initial screening with rapid HIV tests (RHT) into the conventional testing algorithm to screen-out HIV-uninfected infants, thereby reducing the need for costly virologic testing. Methods: Data on HIV prevalence, RHT sensitivity and specificity, and costs were collected from 820 HIV-exposed children (1.5-18 months) attending 2 postnatal screening programs in Uganda during July 2005 to December 2006. Cost-effectiveness models compared the conventional testing algorithm DNA polymerase chain reaction (DNA-PCR with Roche Amplicor v1.5) with a modified algorithm (initial RHT to screen-out HIV-uninfected infants before DNA-PCR). Results: The model estimated that the conventional algorithm would identify 94.3% (91.8%-94.7%) of HIV-infected infants, compared with 87.8% (79.4%-90.5%) for a modified algorithm using RHT (HIV 1/2 Determine) and excluding the need for DNA-PCR for HIV antibody-negative infants. Costs
per infant were $23.47 ($23.32-$23.76) for the conventional algorithm and between $22.75 ($21.89-$23.31) and $7.58 ($6.41-$10.75) for the modified algorithm, depending on infant age and symptoms. Compared with the conventional algorithm, costs per HIV-infected infant identified using the modified algorithm were higher in 1.5- to 3-month-old infants, but significantly lower in 3-month-old and older infants. Models replicating the whole infant testing program showed the modified algorithm would have marginally lower sensitivity, but would reduce total program costs by 27% to 40%, producing an incremental cost-effectiveness ratio of $1489 ($686-$6781) for the conventional versus modified algorithms. Conclusions: Screening infants with RHT before DNA-PCR is cost-effective in infants 3 months old or older. Incorporating RI-IT into early infant testing programs could improve cost-effectiveness and reduce program costs.

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Abstr. OBJECTIVES To describe the pattern of incident illness in children after initiation of antiretroviral therapy (ART) in a large public health sector programme in Lusaka, Zambia. METHODS Systematic chart review to retrospectively extract data from medical records of children (i.e. < 15 years) initiating ART in the Lusaka, Zambia public sector. Incident conditions were listed separately and then grouped according to broad categories. Predictors for incident diagnoses were determined using univariate and multivariable analysis. RESULTS Between May 2004 and June 2006, 1705 HIV-infected children initiated ART. Of these, 1235 (72%) had their medical records reviewed. Median age at ART initiation was 77 months and 554 (45%) were females. Eight hundred and forty-one (68%) children had an incident condition during this period, with a median time of occurrence of 64 days from ART initiation. Twenty-eight incident conditions were documented. When categorized, the most common were mucocutaneous conditions [incidence rate (IR): 70.6 per 100 child-years, 95% CI: 64.5-77.2] and upper respiratory tract infection [IR: 70.1 per 100 child-years; 95% CI: 64.0-76.7]. Children with severe immunosuppression (i.e. CD4 < 10%) were more likely to develop lower respiratory tract infection (16.3% vs. 10.2%; P = 0.003) and mucocutaneous conditions (43.9% vs. 35.3%; P = 0.005) than those with CD4 >= 10%. CONCLUSION There is a high incidence of new illness after ART initiation, emphasizing the importance of close monitoring during this period. Early initiation of ART and use of antimicrobial prophylaxis may also help to reduce the occurrence of such co-morbidities.

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Abstr. A total of 2,570 apparently healthy human immunodeficiency virus-negative adults from the six geopolitical zones in the country were enrolled in our study in 2006. The samples were assayed using the Cyflow technique. Data were analyzed using the Statistical Package for Social Scientists (SPSS). The majority (64%) of the participants had CD4 counts within the range of 501 to 1,000 cells/μl. The reference range for CD4 was 365 to 1,571 cells/μl, while the reference range for CD8 was 145 to 884 cells/μl.

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**Abstr.** In many settings, HIV infected children are looked after with limited access to CD4 cell count or viral load. The decision to initiate antiretroviral therapy (ART) is made clinically, based on the WHO paediatric staging criteria, which were revised in 2006. Results of using new and old criteria were compared. Of 694 children, 626 (90.2%) fulfilled criteria to start ART when applying the new WHO staging guidelines, whereas 330 (47.6%) children were eligible for ART when using the old WHO criteria. This signifies a marked rise in the number of paediatric patients qualifying for ART on clinical grounds.

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**Abstr.** Objective: To determine the acceptability and feasibility of universal HIV testing of 6-week-old infants attending immunization clinics to achieve early diagnosis of HIV and referral for HIV treatment and care services. Design: An observational cohort with intervention. Methods: Routine HIV testing of infants was offered to all mothers bringing infants for immunizations at three clinics in KwaZulu Natal. Blood samples were collected by heel prick onto filter paper. Dried blood spots were tested for HIV antibodies and, if present, were tested for HIV DNA by PCR. Exit interviews were requested of all mothers irrespective of whether they had agreed to infant testing or not. Results: Of 646 mothers bringing infants for immunizations, 584 (90.4%) agreed to HIV testing of their infant and 332 (56.8%) subsequently returned for results. Three hundred and thirty-two of 646 (51.4%) mothers and infants thereby had their HIV status confirmed or reaffirmed by the time the infant was 3 months of age. Overall, 247 of 584 (42.3%) infant dried blood spot samples had HIV antibodies indicating maternal HIV status. Of these, 54 (21.9%) samples were positive for HIV DNA by PCR. This equates to 9.2% (54/584) of all infants tested. The majority of mothers interviewed said they were comfortable with testing of their infant at immunization clinics and would recommend it to others. Conclusion: Screening of all infants at immunization clinics is acceptable and feasible as a means for early identification of HIV-infected infants and referral for antiretroviral therapy.

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**Notes.** Editorial Commentary about Bruyand paper (see above).

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Abstr. Background: The scarcity of physicians in sub-Saharan Africa - particularly in rural clinics staffed only by non-physician health workers - is constraining access to HIV treatment, as only they are legally allowed to start antiretroviral therapy in the HIV-positive patient. Here we present a pilot study from Uganda assessing agreement between non-physician clinicians (nurses and clinical officers) and physicians in their decisions as to whether to start therapy. Methods: We conducted the study at 12 government antiretroviral therapy sites in three regions of Uganda, all of which had staff trained in delivery of antiretroviral therapy using the WHO Integrated Management of Adult and Adolescent Illness guidelines for chronic HIV care. We collected seven key variables to measure patient assessment and the decision as to whether to start antiretroviral therapy, the primary variable of interest being the Final Antiretroviral Therapy Recommendation. Patients saw either a clinical officer or nurse first, and then were screened identically by a blinded physician during the same clinic visit. We measured inter-rater agreement between the decisions of the non-physician health workers and physicians in the antiretroviral therapy assessment variables using simple and weighted Kappa analysis. Results: Two hundred fifty-four patients were seen by a nurse and physician, while 267 were seen by a clinical officer and physician. The majority (> 50%) in each arm of the study were in World Health Organization Clinical Stages I and II and therefore not currently eligible for antiretroviral therapy according to national antiretroviral therapy guidelines. Nurses and clinical officers both showed moderate to almost perfect agreement with physicians in their Final Antiretroviral Therapy Recommendation (unweighted kappa = 0.59 and kappa = 0.91, respectively). Agreement was also substantial for nurses versus physicians for assigning World Health Organization Clinical Stage (weighted kappa = 0.65), but moderate for clinical officers versus physicians (kappa = 0.44). Conclusion: Both nurses and clinical officers demonstrated strong agreement with physicians in deciding whether to initiate antiretroviral therapy in the HIV patient. This could lead to immediate benefits with respect to antiretroviral therapy scale-up and decentralization to rural areas in Uganda, as non-physician clinicians - particularly clinical officers - demonstrated the capacity to make correct clinical decisions to start antiretroviral therapy. These preliminary data warrant more detailed and multicountry investigation into decision-making of non-physician clinicians in the management of HIV disease with antiretroviral therapy, and should lead policymakers to more carefully explore task-shifting as a shorter-term response to addressing the human resource crisis in HIV care and treatment.

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Abstr. Primary or transmitted antiretroviral drug resistance mutations pose a significant obstacle for optimizing antiviral treatment. When present at low-levels, resistance mutations are less likely to be detected by standard genotyping assays. This study utilizes a novel rolling circle amplification (RCA) method using padlock probes to achieve the sensitive, specific and low-level detection of the NNRTI resistance K103N from 59
HIV+ treatment-naive patients from Beijing, China. Using standard genotyping methods, primary drug resistance mutations to either protease or RT inhibitors were found in 25% (15/59) of patients attending hospital clinics in Beijing. Among these 15 patients with antiretroviral (ARV) resistance mutations, standard sequence-based genotyping revealed that most (10/15) had the 103N. Using a highly sensitive RCA assay, 5 more patients among the 59 treatment-naive cohort were found to have the 103N, but at low-levels, leading to an overall rate of 103N at 25.4% (15/59) in this population. The high prevalence of the 103N suggests that baseline resistance testing should be performed before treatment in this population. Importantly, the new RCA technology allows large-scale, sensitive detection of drug resistance mutations, including detection of minority populations with minimal equipment requirement. (C) 2009 Elsevier B.V. All rights reserved.

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Abstr. Background: China's National Free Antiretroviral Treatment Program began in 2002 and, by August 2008, included more than 52 000 patients. Objective: To report 5-year outcomes on adult mortality and immunologic treatment failure rates and risk factors. Design: Open cohort analysis of a prospectively collected, observational database. Setting: China. Patients: All patients in the national treatment database from June 2002 to August 2008. Patients were excluded if they had not started triple therapy or had missing treatment regimen information. Intervention: Antiretroviral therapy according to Chinese national treatment guidelines. Measurements: Mortality rate and immunologic treatment failure rate, according to World Health Organization criteria. Results: Of 52 191 patients, 48 785 were included. Median age was 38 years, 58% were men, 53% were infected through plasma or blood, and the median baseline CD4 cell count was 0.118 x 10(9) cells/L. Mortality was greatest during the first 3 months of treatment (22.6 deaths per 100 person-years) but decreased to a steady rate of 4 to 5 deaths per 100 person-years after 6 months and maintained this rate over the subsequent 4.5 years. The strongest mortality risk factors were a baseline CD4 cell count less than 0.050 x 10(9) cells/L (adjusted hazard ratio [HR] compared with a count >= 0.200 x 10(9) cells/L, 3.3 [95% CI, 2.9 to 3.8]) and having 4 to 5 baseline symptom categories (adjusted HR compared with no baseline symptom categories, 3.4 [CI, 2.9 to 4.0]). Treatment failure was determined among 31 070 patients with 1 or more follow-up CD4 cell counts. Overall, treatment failed for 25% of patients (12.0 treatment failures per 100 person-years), with the cumulative treatment failure rate increasing to 50% at 5 years. Limitation: Immunologic treatment failure does not necessarily correlate well with virologic treatment failure. Conclusion: The National Free Antiretroviral Treatment Program reduced mortality among adult patients in China with AIDS to rates similar to those of other low-or middle-income countries. A cumulative immunologic treatment failure rate of 50% after 5 years, due to the limited availability of second-line regimens, is of great concern.

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