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Buchacz K, Weidle PJ, Moore D, Were W, Mermin J, Downing R, Kigozi A, Borkowf CB, Ndazinia V, Brooks JT. **Changes in lipid profile over 24-months among adults on first-line highly active Antiretroviral therapy in the home-based AIDS care program in rural Uganda.** *Journal of Acquired Immune Deficiency Syndromes* 2008;47(3):304-311.

Abstr. Background: Use of highly active antiretroviral therapy (HAART) has been linked to dyslipidemia and increased risk of cardiovascular disease (CVD) in HIV-infected patients in industrialized countries. The effects of HAART on lipid metabolism among sub-Saharan Africans, for whom access to antiretroviral therapy is expanding, remain largely unknown. Methods: From July 2003 to May 2004, 987 antiretroviral-naïve patients with symptomatic HIV disease or a CD4 count < 250 cells/mm³ were started on HAART in the Home-Based AIDS Care (HBAC) Program in Tororo, Uganda. The HBAC Program provided weekly drug delivery and field-based clinical monitoring. Nonfasting repository sera from a subset of 374 patients were analyzed for levels of total cholesterol (TC), direct low-density lipoprotein cholesterol (LDL-c), direct high-density lipoprotein cholesterol (HDL-c), and triglycerides (TG) at baseline (before HAART) and after 12 and 24 months of HAART using Randox enzymatic kits (Crumlin, United Kingdom). Results: The 374 patients evaluated (49% women, mean age = 39 years, CD4 count = 124 cells/mm³, body mass index = 19.7 kg/m²) received initial HAART composed of stavudine, lamivudine, and either nevirapine (365 patients [98%]) or efavirenz (9 patients [2%]). During 24 months, 99 (26%) patients had single drug substitutions from stavudine to zidovudine and 27 (7%) had single drug substitutions from nevirapine to efavirenz. At baseline, the mean serum lipid concentrations were 120 mg/dL for TC, 53 mg/dL for LDL-c, 29 mg/dL for HDL-c, and 123 mg/dL for TG; values were generally comparable for men and women. During 24 months of treatment, TC increased by a mean of 31 mg/dL, LDL-c by a mean of 26 mg/dL, and HDL-c by a mean of 19 mg/dL, whereas the TC/HDL-c ratio decreased from a mean of 4.6 to 3.4 (all changes, P < 0.001). TG levels initially decreased and then returned to baseline levels by 24 months. At baseline and 24 months, respectively, TC was ≥ 200 mg/dL for 2% and 10% of patients, LDL-c was ≥ 130 mg/dL for 1% and 6%, HDL-c was < 40 mg/dL for 88% and 41%, and TG were ≥ 150 mg/dL for 23% and 20%. Conclusions: Rural Ugandans with advanced HIV disease initiating nevirapine- or efavirenz-based HAART experienced infrequent elevations in TC, LDL-c, and TG at baseline and after 24 months of therapy. Increases in HDL-c levels were substantial and proportionally greater than increases in TC or LDL-c levels. The risk of CVD and how it is affected by lipid changes in this rural African population are unknown. However, the changes we observed after 24 months of HAART seem unlikely to increase the risk of CVD.

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Chersich MF, Luchters SMF, Othigo MJ, Yard E, Mandaflya K, Temmerman M. **HIV testing and counselling for women attending child health clinics: an opportunity for entry to prevent mother-to-child transmission and HIV treatment.** *International Journal of STD & AIDS* 2008;19(1):42-46.

Abstr. This study assessed the potential for HIV testing at child health clinics to increase knowledge of HIV status, and entry to infant feeding counselling and HIV treatment. At a provincial hospital in Mombasa, Kenya, HIV testing and counselling were offered to women bringing their child for immunization or acute care services. Most women said HIV testing should be offered in these clinics (472/493, 95.7%), with many citing the benefits of regular testing and entry to prevent mother-to-child transmission. Of 500 women, 416 (83.4%) received test results, 97.6% on the same day. After 50 participants, point-of-care testing replaced laboratory-based rapid testing. Uptake increased 2.6 times with point-of-care testing (95% confidence interval = 1.4-5.1; P = 0.003). Of 124 women who had not accessed HIV testing during pregnancy, 98 tested in the study (79.0%). Measured by uptake and attitudes, HIV testing in child health clinics is acceptable. This

could optimize entry into HIV treatment, infant feeding counselling and family planning services.

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Cherutich P, Inwani I, Nduati R, Mbori Ngacha D. **Optimizing paediatric HIV care in Kenya: challenges in early infant diagnosis.** Bulletin of the World Health Organization 2008;86(2):155-160.

Abstr. Problem In 2003, the goal of the Kenyan Ministry of Health was to avail antiretroviral treatment (ART) to 50% of the estimated 250 000 eligible individuals by the end of 2005. By July 2005, 45 000 adults and more than 2000 children were on treatment. A study was conducted to determine the barriers to identification of HIV-infected children. Approach Existing government policies were reviewed and the ART register of the Kenya National AIDS Control Programme was used to identify facilities providing ART. This paper reports the findings around diagnosis and staging of HIV infection in children. Local setting At the time of the study, 58 health facilities were providing ART to children. Only one institution had achieved universal HIV testing in the antenatal clinics. Six facilities systematically followed up HIV-exposed children. HIV antibody testing was not readily available to the children. Although four research centres were capable of carrying out diagnostic HIV polymerase chain reaction (PCR), the services were restricted to research purposes. Other constraints were inadequate physical infrastructure, inadequate systems for quality control in the laboratories and shortage of staff. Lessons learnt The policy framework to support identification of HIV-infected children had been established, albeit with narrow focus on sick children. The assessment identified the weaknesses in the structures for systematic diagnosis of HIV through laboratory or clinical-based algorithms. The researchers concluded that health staff training and implementation of a systematic standard approach to identification of HIV-infected children is urgently required.

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Chopra M, Rollins N. **Infant feeding in the time of HIV: rapid assessment of infant feeding policy and programmes in four African countries scaling up prevention of mother to child transmission programmes.** Archives of Disease in Childhood 2008;93(4):288-291.

Abstr. Objective: To assess the infant feeding components of prevention of mother to child HIV transmission (PMTCT) programmes. Methods: Assessments were performed across Botswana, Kenya, Malawi and Uganda. 29 districts offering PMTCT were selected by stratified random sampling with rural and urban strata. All health facilities in the selected PMTCT district were assessed. The facility level manager and the senior nurse in charge of maternal care were interviewed. 334 randomly selected health workers involved in the PMTCT programme completed self-administered questionnaires. 640 PMTCT counselling observations were carried out and 34 focus groups were conducted amongst men and women. Results: Most health workers (234/334, 70%) were unable to correctly estimate the transmission risks of breastfeeding irrespective of exposure to PMTCT training. Infant feeding options were mentioned in 307 of 640 (48%) observations of PMTCT counselling sessions, and in only 35 (5.5%) were infant feeding issues discussed in any depth; of these 19 (54.3%) were rated as poor. Several health workers also reported receiving free samples of infant formula in contravention of the International Code on Breastmilk Substitutes. National HIV managers stated they were unsure about infant feeding policy in the context of HIV. Finally, there was an almost universal belief that an HIV positive mother who breastfeeds her child will always infect the child and intentional avoidance of breastfeeding by the mother indicates that she is

HIV positive. Conclusion: These findings underline the need to implement and support systematic infant feeding policies and programme responses in the context of HIV programmes.

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Delfraissy JFO, Flandre P, Delaugerre C, Ghosn J, Horban A, Girard PM, Norton M, Rouzioux C, Taburet AM, Cohen Codar I, Van PN, Chauvin JP. **Lopinavir/ritonavir monotherapy or plus zidovudine and lamivudine in antiretroviral-naive HIV-infected patients.** AIDS 2008;22(3):385-393.

Abstr. Background: Guidelines for the use of antiretroviral agents for HIV-1 infection recommend combining at least three agents. The toxicity, cost, and complexity of such regimens warrant the search for other options. Methods: MONARK is a prospective, open-label, randomized, 96-week trial comparing the safety and efficacy of lopinavir/ritonavir monotherapy with a standard lopinavir/ritonavir plus zidovudine and lamivudine regimen as an initial treatment regimen in HIV-infected patients with HIV-RNA levels less than 100 000 copies/ml. The primary endpoint was the proportion of patients with HIV-1-RNA levels below 400 copies/ml at week 24 and below 50 copies/ml at week 48. Results: Eighty-three and 53 patients were randomly assigned and exposed in the monotherapy and triple-drug groups, respectively. At week 48, by an intent-to-treat analysis, 53 of 83 patients (64%) in the monotherapy group and 40 of 53 patients (75%) in the triple-drug group achieved the primary endpoint ($P=0.19$). The on-treatment analysis indicates that 80 and 95% of patients reached the primary endpoint in the monotherapy and triple-drug groups, respectively ($P=0.02$). In the monotherapy arm, protease inhibitor-associated resistance mutations were seen in three of the 21 patients qualifying for genotypic resistance testing, with a modest impact on lopinavir susceptibility. None of the serious reported adverse events were considered to be related to study treatment. Conclusion: Our results suggest that lopinavir/ritonavir monotherapy demonstrates lower rates of virological suppression when compared with lopinavir/ritonavir triple therapy and therefore should not be considered as a preferred treatment option for widespread use in antiretroviral-naive patients.

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Gasasira AF, Kanya MR, Achan J, Mebrahtu T, Kalyango JN, Ruel T, Charlebois E, Staedke SG, Kekitiinwa A, Rosenthal PJ, Havlir D, Dorsey G. **High risk of neutropenia in HIV-infected children following treatment with artesunate plus amodiaquine for uncomplicated malaria in Uganda.** Clinical Infectious Diseases 2008;46(7):985-991.

Abstr. Background. Artemisinin-based combination therapies are rapidly being adopted for the treatment of malaria in Africa; however, there are limited data on their safety and efficacy among human immunodeficiency virus (HIV)-infected populations. Methods. We compared malaria treatment outcomes between cohorts of HIV-infected and HIV-uninfected children in Uganda who were observed for 18 and 29 months, respectively. Malaria was treated with artesunate plus amodiaquine, and outcomes were assessed using standardized guidelines. HIV-infected children received trimethoprim-sulfamethoxazole prophylaxis and antiretroviral therapy in accordance with current guidelines. Results. Twenty-six HIV-infected participants experiencing 35 episodes of malaria and 134 HIV-uninfected children experiencing 258 episodes of malaria were included in the study. Twelve HIV-infected children were receiving antiretroviral therapy, 11 of whom were receiving zidovudine. Malaria treatment was highly efficacious in both the HIV-infected and HIV-uninfected cohorts (28-day risk of recrudescence, 0% and 3.6%, respectively); however, there was a trend towards increased risk of recurrent malaria among the HIV-uninfected children (2.9% vs. 13.2%;). Importantly, the risk of neutropenia 14 days after initiation of treatment with artesunate plus P = .08

amodiaquine was higher among HIV-infected children than among HIV-uninfected children (45% vs. 6%; $P < .001$). The severity of all episodes of neutropenia in HIV-uninfected children was mild to moderate, and 16% of episodes of neutropenia in the HIV-infected cohort were severe or life-threatening (neutrophil count, <750 cells/mm³). In the HIV-infected cohort, the risk of neutropenia was significantly higher among children who received antiretroviral therapy than among those who did not receive antiretroviral therapy (75% vs. 26%; $P = .001$). Conclusions. Artesunate plus amodiaquine was highly efficacious for malaria treatment in HIV-infected children but was associated with a high risk of neutropenia, especially in the context of concurrent antiretroviral use. Our findings highlight an urgent need for evaluation of alternative antimalarial therapies for HIV-infected individuals.

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Korenromp EL, Kayondo JK. **Reduced mortality with home-based HIV treatment in Uganda** [Editorial]. *Lancet* 2008;371(9614):703-705.

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Mehta U, Durrheim DN, Blockman M, Kredo T, Gounden R, Barnes KI. **Adverse drug reactions in adult medical inpatients in a South African hospital serving a community with a high HIV/AIDS prevalence: prospective observational study.** *British Journal of Clinical Pharmacology* 2008;65(3):396-406.

Abstr. AIMS To describe the frequency, nature and preventability of community-acquired and hospital-acquired adverse drug reactions (ADRs) in a South African hospital serving a community with a high prevalence of human immunodeficiency virus (HIV)/ acquired immunodeficiency syndrome. METHODS A 3-month prospective observational study of 665 adults admitted to two medical wards. RESULTS Forty-one (6.3%) patients were admitted as a result of an ADR and 41 (6.3%) developed an ADR in hospital. Many of the ADRs (46.2%) were considered preventable, although less likely to be preventable in HIV-infected patients than in those with negative or unknown HIV status (community-acquired ADRs 2/24 vs. 35/42; $P < 0.0001$; hospital-acquired ADRs 3/25 vs. 14/26; $P = 0.003$). Patients admitted with ADRs were older than patients not admitted with an ADR (median 53 vs. 42 years, $P = 0.003$), but 60% of community-acquired ADRs at hospital admission were in patients < 60 years old. Among patients < 60 years old, those HIV infected were more likely to be admitted with an ADR [odds ratio (OR) 2.32, 95% confidence interval (CI) 1.17, 4.61; $P = 0.017$]. Among HIV-infected patients, those receiving antiretroviral therapy (ART) were more likely to be admitted with an ADR than those not receiving ART (OR 10.34, 95% CI 4.50, 23.77; $P < 0.0001$). No ART-related ADRs were fatal. Antibiotics and drugs used for opportunistic infections were implicated in two-thirds of hospital-acquired ADRs. CONCLUSIONS ADRs are an important, often preventable cause of hospitalizations and inpatient morbidity in South Africa, particularly among the elderly and HIV-infected. Although ART-related injury contributed to hospital admissions, many HIV-related admissions were among patients not receiving ART, and many ADRs were associated with medicines used for managing opportunistic infections.

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Mermin J, Were W, Ekwaru JP, Moore D, Downing R, Behumbiize P, Lule JR, Coutinho A, Tappero J, Bunnell R. **Mortality in HIV-infected Ugandan adults receiving antiretroviral treatment and survival of their HIV-uninfected children: a prospective cohort study.** *Lancet* 2008;371(9614):752-759.

Abstr. Background Antiretroviral therapy (ART) is increasingly available in Africa, but physicians and clinical services are few. We therefore assessed the effect of a home-

based ART programme in Uganda on mortality, hospital admissions, and orphanhood in people with HIV-1 and their household members. Methods In 2001, we enrolled and followed up 466 HIV-infected adults and 1481 HIV-uninfected household members in a prospective cohort study. After 5 months, we provided daily co-trimoxazole (160 mg trimethoprim and 800 mg sulfamethoxazole) prophylaxis to HIV-infected participants. Between May, 2003, and December, 2005, we followed up 138 infected adults who were eligible and 907 new HIV-infected participants and their HIV-negative household members in a study of ART (mainly stavudine, lamivudine, and nevirapine). Households were visited every week by lay providers, and no clinic visits were scheduled after enrolment. We compared rates of death, hospitalisation, and orphanhood during different study periods and calculated the number needed to treat to prevent an outcome. Findings 233 (17%) of 1373 participants with HIV and 40 (1%) of 4601 HIV-uninfected household members died. During the first 16 weeks of ART and co-trimoxazole, mortality in HIV-infected participants was 55% lower than that during co-trimoxazole alone (14 vs 16 deaths per 100 person-years; adjusted hazard ratio 0.45, 95% CI 0.27-0.74, $p=0.0018$), and after 16 weeks, was reduced by 92% (3 vs 16 deaths per 100 person-years; 0.08, 0.06-0.13, $p<0.0001$). Compared with no intervention, ART and co-trimoxazole were associated with a 95% reduction in mortality in HIV-infected participants (5 vs 27 deaths per 100 person-years; 0.05, 0.03-0.08, $p<0.0001$), 81% reduction in mortality in their uninfected children younger than 10 years (0.2 vs 1.2 deaths per 100 person-years; 0.19, 0.06-0.59, $p=0.004$), and a 93% estimated reduction in orphanhood (0.9 vs 12.8 per 100 person-years of adults treated; 0.07, 0.04-0.13, $p<0.0001$). Interpretation Expansion of access to ART and co-trimoxazole prophylaxis could substantially reduce mortality and orphanhood among adults with HIV and their families living in resource-poor settings.

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Reyburn H, Mwakasungula E, Chonya S, Mtei F, Bygbjerg I, Poulsen A, Olomi R. **Clinical assessment and treatment in paediatric wards in the north-east of the United Republic of Tanzania.** Bulletin of the World Health Organization 2008;86(2):132-139.

Abstr. Objective We assessed paediatric care in the 13 public hospitals in the north-east of the United Republic of Tanzania to determine if diagnoses and treatments were consistent with current guidelines for care. Methods Data were collected over a five-day period in each site where paediatric outpatient consultations were observed, and a record of care was extracted from the case notes of children on the paediatric ward. Additional data were collected from inspection of ward supplies and hospital reports. Findings Of 1181 outpatient consultations, basic clinical signs were often not checked; e.g. of 895 children with a history of fever, temperature was measured in 57%, and of 657 of children with cough or dyspnoea only 57 (9%) were examined for respiratory rate. Among 509 inpatients weight was recorded in the case notes in 250 (49%), respiratory rate in 54 (11%) and mental state in 47 (9%). Of 206 malaria diagnoses, 123 (60%) were with a negative or absent slide result, and of these 44 (36%) were treated with quinine only. Malnutrition was diagnosed in 1% of children admitted while recalculation of nutritional Z-scores suggested that between 5% and 10% had severe acute malnutrition; appropriate feeds were not present in any of the hospitals. A diagnosis of HIV-AIDS was made in only two cases while approximately 5% children admitted were expected to be infected with HIV in this area. Conclusion Clinical assessment of children admitted to paediatric wards is disturbingly poor and associated with missed diagnoses and inappropriate treatments. Improved assessment and records are essential to initiate change, but achieving this will be a challenging task.

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Zachariah R, Van Engelgem I, Massaquoi M, Kocholla L, Manzi M, Suleh A, Phillips M, Borgdorff M. **Payment for antiretroviral drugs is associated with a higher rate of patients lost to follow-up than those offered free-of-charge therapy in Nairobi, Kenya.** Transactions of the Royal Society of Tropical Medicine and Hygiene 2008;102(3):288-293.

Abstr. This retrospective analysis of routine programme data from Mbagathi District Hospital, Nairobi, Kenya shows the difference in rates of loss to follow-up between a cohort that paid 500 shillings/month (approximately US\$7) for antiretroviral drugs (ART) and one that received medication free of charge. A total of 435 individuals (mean age 31.5 years, 65% female) was followed-up for 146 person-years: 265 were in the 'payment' cohort and 170 in the 'free' cohort. The incidence rate for Loss to follow-up per 100 person-years was 47.2 and 20.5, respectively (adjusted hazard ratio 2.27, 95% CI 1.21-4.24, P=0.01). Overall risk reduction attributed to offering ART free of charge was 56.6% (95% CI 20.0-76.5). Five patients diluted their ART regimen to one tablet (instead of two tablets) twice daily in order to reduce the monthly cost of medication by half. ALL these patients were from the payment cohort. Payment for ART is associated with a significantly higher rate of loss to follow-up, as some patients might be unable to sustain payment over time. In resource-limited settings, ART should be offered free of charge in order to promote treatment compliance and prevent the emergence of drug resistance.

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