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Beck EJ, Vitoria M, Mandalia S, Crowley S, Gilks CF, Souteyrand Y. **National adult antiretroviral therapy guidelines in resource-limited countries: concordance with 2003 WHO guidelines?** AIDS 2006;20(11):1497-1502.

Abstr. Aims: To investigate the existence of national adult antiretroviral therapy (ART) guidelines in 43 World Health Organization (WHO) '3 by 5' focus countries and compare their content with the 2003 WHO ART guidelines. Methods: Questionnaires covered initiation of ART, selection of first or second-line ART, monitoring treatment response and toxicity and dissemination of national guidelines. Weighted concordance scores were created and country scores correlated with national indicators and WHO recommendations. Results: Thirty-nine (91%) countries returned questionnaires, three of which had no national ART guidelines. Of the 36, 16 (44%) recommended to start ART based on WHO clinical staging criteria and CD4 cell count or T lymphocyte count, 12 (33%) WHO clinical staging criteria and CD4 cell count, four (11%) only CD4 cell counts. 35 (97%) recommended a standard first-line regimen and 24 (67%) preferred stavudine + lamivudine + nevirapine; 33 (92%) recommended second-line regimens, and 24 (60%) preferred abacavir + didanosine + lopinavir/ritonavir. Thirty-one (94%) recommended CD4 cell count, possibly combined with other indicators, to monitor ART. Concordance scores were higher in countries with lower health expenditure per capita ($P = 0.009$) and lower GDP per capita ($P < 0.03$). Median concordance scores for starting ART was 100 [interquartile range (IQR), 67 to 100]; first line therapy, 70 (IQR, 60 to 80); second-line regimens, 45 (IQR, 27 to 55) and for laboratory investigations, 80 (IQR, 80 to 100). Conclusions: Most countries had developed national ART guidelines as part of a comprehensive national HIV program. Concordance with WHO recommendations was strong on starting first-line ART regimens and routine monitoring but lower for second-line recommendations.

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Bisson GP, Gross R, Strom JB, Rollins C, Bellamy S, Weinstein R, Friedmand H, Dickinson D, Frank I, Strom BL, Gaolathe T, Ndwapi N. **Diagnostic virologic accuracy of CD4 cell count increase for response after initiating highly active antiretroviral therapy.** AIDS 2006;20(12):1613-1619.

Abstr. Objective: To derive and internally validate a clinical prediction rule for virologic response based on CD4 cell count increase after initiation of HAART in a resource-limited setting. Design and methods: A retrospective cohort study at two HIV care clinics in Gaborone, Botswana. The participants were previously treatment-naive HIV-1-infected individuals initiating HAART. The main outcome measure was a plasma HIV-1 RNA level (viral load) ≤ 400 copies/ml (i.e. undetectable) 6 months after initiating HAART. Results: The ability of CD4 cell count increase to predict an undetectable viral load was significantly better in those with baseline CD4 cell counts ≤ 100 cells/ μ l [area under the ROC curve (AUC), 0.78; 95% confidence interval (CI), 0.67-0.89; versus AUC, 0.60; 95% CI, 0.48-0.71; $P=0.018$]. The sensitivity, specificity, and positive and negative predictive values of a CD4 cell count increase of ≥ 50 cells/ μ l for an undetectable viral load in those with baseline CD4 cell counts ≤ 100 cells/ μ l were 93.1, 61.3, 92.5 and 63.3%, respectively. Alternatively, these values were 47.8, 87.1, 95.0 and 24.5%, respectively, if a increase in CD4 cell count of ≥ 150 cells/ μ l was used. Conclusions: CD4 cell count increase after initiating HAART has only moderate discriminative ability in identifying patients with an undetectable viral load, and the predictive ability is lower in patients with lower baseline CD4 cell counts. Although HIV treatment programs in resource-constrained settings could consider the use of CD4 cell count increases to triage viral load testing, more accurate approaches to monitoring virologic failure are urgently needed.

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Doherty T, Chopra M, Nkonki L, Jackson D, Persson LA. **A longitudinal qualitative study of infant-feeding decision making and practices among HIV-Positive women in South Africa.** Journal of Nutrition 2006;136(9):2421-2426.

Abstr. This study examined the challenges that HIV-positive women face at different stages of early infant feeding using a longitudinal, qualitative design. The study explored factors influencing infant-feeding decision-making and behavior of HIV positive mothers and identified characteristics of women and their environments that contributed to success in maintaining exclusivity of their infant feeding practices. The study was undertaken at 3 sites in South Africa. Participants consisted of a purposive sample of 27 women who had a positive HIV test result during antenatal care and were intending to either exclusively breast-feed or exclusively formula-feed their infants. Women were interviewed once antenatally and at 1, 4, 6, and 12 wk postpartum. Just under one-half of the women who initiated breast-feeding maintained exclusivity and over two-thirds of the women who initiated formula-feeding maintained exclusivity. Key characteristics of women who achieved success in exclusivity included the ability to resist pressure from the family to introduce other fluids and to recall key messages on mother-to-child transmission risks and mixed feeding. Among women who maintained exclusive breast-feeding, a strong belief in the benefits of breast-feeding and a supportive home environment was important. For women

using formula milk, having resources such as electricity, a kettle, and flask made feeding at night easier. Support for infant feeding that extends beyond the antenatal period is important to enable mothers to cope with new challenges and pressures at critical times during the early postpartum period.

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Egger M. **Rates of disease progression according to initial highly active antiretroviral therapy regimen: A collaborative analysis of 12 prospective cohort studies.** *Journal of Infectious Diseases* 2006;194(5):612-622.

Abstr. Background. No large clinical end-point trials have been conducted comparing regimens among human immunodeficiency virus type 1-positive persons starting antiretroviral therapy. We examined clinical progression according to initial regimen in the Antiretroviral Therapy Cohort Collaboration, which is based on 12 European and North American cohort studies. Methods. We analyzed progression to death from any cause and to AIDS or death (AIDS/death), comparing efavirenz (EFV), nevirapine (NVP), nelfinavir, idinavir, ritonavir (RTV), RTV-boosted protease inhibitors (PIs), saquinavir, and abacavir. We also compared nucleoside reverse-transcriptase inhibitor pairs: zidovudine/lamivudine (AZT/3TC), stavudine (D4T)/3TC, D4T/didanosine (DDI), and others. Results. A total of 17,666 treatment-naïve patients, 55,622 person-years at risk, 1617 new AIDS events, and 895 deaths were analyzed. Compared with EFV the adjusted hazard ratio (HR) for AIDS/death was 1.28 (95% confidence interval [CI], 1.03-1.60) for NVP, 1.31 (95% CI, 1.01-1.71) for RTV and 1.45 (95% CI, 1.15-1.81) for RTV-boosted PIs. For death, the adjusted HR for NVP was 1.65 (95% CI, 1.16-2.36). The adjusted HR for death for D4T/3TC was 1.35 (95% CI, 1.14-1.59), compared with AZT/3TC. Conclusions. Outcomes may vary across initial regimens. Results are observational and may have been affected by bias due to unmeasured or residual confounding. There is a need for large, randomized, clinical end-point trials.

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Fryland M, Chaillet P, Zachariah R, Barnaba A, Bonte L, Andereassen R, Charrondiere S, Teck R, Didakus O. **The Partec CyFlow Counter (R) could provide an option for CD4+T-cell monitoring in the context of scaling-up antiretroviral treatment at the district level in Malawi.** *Transactions of the Royal Society of Tropical Medicine and Hygiene* 2006;100(10):980-985.

Abstr. A study was conducted in rural Malawi to verify (a) whether the Partec CyFlow Counter(R) for CD4+ T-cell lymphocyte counting in HIV-positive individuals could be introduced into a district hospital. laboratory and (b) whether it would produce CD4 counts of acceptable quality. CD4+ cell, counting was performed using the Partec CyFlow Counter and the results were compared with a reference method (FACsCount). A total of 311 blood samples were analysed and the correlation coefficient for the CyFlow Counter was 0.92 (95% CI 0.89-0.95). Mean CD4 counts using the Partec and the reference methods were 308.2cells/mu l and 316.9cells/mu l, respectively. The mean difference in CD4 count values was -8.68cells/mu l (95% CI -18.8 to 1.4). Mean intra-run variation was -6.84cells/mu l (95% CI -12.9 to 0.79). In the district laboratory setting, the instrument could accommodate up to 75 blood samples per technician per day. After being trained, local laboratory staff found the CyFlow Counter procedures simple to run and the instrument easy to manipulate. The Partec CyFlow Counter produces sufficiently reliable results and the instrument appears robust under field conditions. It could provide a new option for introducing routine CD4+ cell monitoring at the district level. in the context of scaling-up antiretroviral therapy in Malawi.

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Goldie SJ, Yazdanpanah Y, Losina E, Weinstein MC, Anglaret X, Walensky RP, Hsu HE, Kimmel A, Holmes C, Kaplan JE, Freedberg KA. **Cost-effectiveness of HIV treatment in resource-poor settings - The case of Cote d'Ivoire.** *New England Journal of Medicine* 2006;355(11):1141-1153.

Abstr. BACKGROUND: As antiretroviral therapy is increasingly used in settings with limited resources, key questions about the timing of treatment and use of diagnostic tests to guide clinical decisions must be addressed. METHODS: We assessed the cost-effectiveness of treatment strategies for a cohort of adults in Cote d'Ivoire who were infected with the human immunodeficiency virus (HIV) (mean age, 33 years; CD4 cell count, 331 per cubic millimeter; HIV RNA level, 5.3 log copies per milliliter). Using a computer-based simulation model that incorporates the CD4 cell count and HIV RNA level as predictors of disease progression, we compared the long-term clinical and economic outcomes associated with no treatment, trimethoprim-sulfamethoxazole prophylaxis alone, antiretroviral therapy alone, and prophylaxis with antiretroviral therapy. RESULTS: Undiscounted gains in life expectancy ranged from 10.7 months with antiretroviral therapy and prophylaxis initiated on the basis of clinical criteria to 45.9 months with antiretroviral therapy and prophylaxis initiated on the basis of CD4 testing and clinical criteria, as compared with trimethoprim-sulfamethoxazole prophylaxis alone. The incremental cost per year of life gained was \$240 (in 2002 U.S. dollars) for prophylaxis alone, \$620 for antiretroviral therapy and prophylaxis without CD4 testing, and \$1,180 for antiretroviral therapy and prophylaxis with CD4 testing, each

compared with the next least expensive strategy. None of the strategies that used antiretroviral therapy alone were as cost-effective as those that also used trimethoprim-sulfamethoxazole prophylaxis. Life expectancy was increased by 30% with use of a second line of antiretroviral therapy after failure of the first-line regimen. CONCLUSIONS: A strategy of trimethoprim-sulfamethoxazole prophylaxis and antiretroviral therapy, with the use of clinical criteria alone or in combination with CD4 testing to guide the timing of treatment, is an economically attractive health investment in settings with limited resources.

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Kiarie JN, Farquhar C, Richardson BA, Kabura MN, John FN, Nduati RW, John Stewart GC. **Domestic violence and prevention of mother-to-child transmission of HIV-1**. AIDS 2006;20(13):1763-1769.

Abstr. Objectives: To determine the prevalence of life-time domestic violence by the current partner before HIV-1 testing, its impact on the uptake of prevention of mother-to-child transmission (PMTCT) interventions and frequency after testing. Design A prospective cohort. Methods Antenatally, women and their partners were interviewed regarding physical, financial, and psychological abuse by the male partner before HIV-1 testing and 2 weeks after receiving results. Results Before testing, 804 of 2836 women (28%) reported previous domestic violence, which tended to be associated with increased odds of HIV-1 infection [univariate odds ratio (OR) 1.7, 95% confidence interval (CI) 1.3-2.2; $P < 0.0001$, adjusted OR 1.2, 95% CI 0.9-1.6; $P = 0.1$], decreased odds of coming with partners for counseling (adjusted OR 0.7, 95% CI 0.5-1.0; $P = 0.04$), and decreased odds of partner notification (adjusted OR 0.7, 95% CI 0.5-1.1; $P = 0.09$). Previous domestic violence was not associated with a reduced uptake of HIV-1 counseling, HIV-1 testing, or nevirapine. After receiving results, 15 out of 1638 women (0.9%) reported domestic violence. After notifying partners of results, the odds of HIV-1-seropositive women reporting domestic violence were 4.8 times those of HIV-1-seronegative women (95% CI 1.4-16; $P=0.01$). Compared with women, men reported similar or more male-perpetrated domestic violence, suggesting a cultural acceptability of violence. Conclusion Domestic violence before testing may limit partner involvement in PMTCT. Although infrequent, immediate post-test domestic violence is more common among HIV-1-infected than uninfected women. Domestic violence prevention programmes need to be integrated into PMTCT, particularly for HIV-1-seropositive women.

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Lawn SD, Myer L, Bekker LG, Wood R. **Burden of tuberculosis in an antiretroviral treatment programme in sub-Saharan Africa: impact on treatment outcomes and implications for tuberculosis control**. AIDS 2006;20(12):1605-1612.

Abstr. Objectives: To determine burden and risk factors for tuberculosis (TB) in an antiretroviral treatment (ART) programme and its impact on ART outcomes. Design: Prospective cohort study. Methods: Prevalent TB was assessed at baseline and incident TB was ascertained prospectively over 3 years among 944 patients accessing a community-based ART programme in South Africa. Results: At enrollment, median CD4 cell count was 96 cells/ μl and 52% of patients had a previous history of TB. Prevalent TB (current antituberculosis treatment or active TB) was present in 25% and was strongly associated with advanced immunodeficiency. During 782 person-years of ART, 81 cases of TB were diagnosed. The incidence was 22.1/100 person-years during the first 3 months of ART and decreased to an average of 4.5/100 person-years during the second and third years. In multivariate analysis, risk of incident TB during follow-up was only associated with the current absolute CD4 cell count at that time point; an increase of 100 cells/ μl was associated with a 25% lower risk ($P = 0.007$). Although prevalent and incident TB were associated with greater than two-fold increased mortality risk, they did not compromise immunological and virological outcomes among survivors at 48 weeks. Conclusions: Late initiation of ART was associated with a major burden of TB in this ART programme. TB reduced survival but did not impair immunovirological outcomes. Reductions in TB incidence during ART were dependent on CD4 cell count; however, after 3 years of treatment, rates were still 5- to 10-fold higher than among non-HIV-infected people. Earlier initiation of ART may reduce this burden of TB.

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Lawn SD, Myer L, Harling G, Orrell C, Bekker LG, Wood R. **Determinants of mortality and nondeath losses from an antiretroviral treatment service in South Africa: Implications for program evaluation**. Clinical Infectious Diseases 2006;43(6):770-776.

Abstr. Background. The scale-up of antiretroviral treatment (ART) services in resource-limited settings requires a programmatic model to deliver care to large numbers of people. Understanding the determinants of key outcome measures-including death and nondeath losses - would assist in program evaluation and development. Methods. Between September 2002 and August 2005, all in-program (pretreatment and on-treatment) deaths and

nondeath losses were prospectively ascertained among treatment-naive adults (n = 1235) who were enrolled in a community-based ART program in South Africa. Results. At study censorship, 927 patients had initiated ART after a median of 34 days after enrollment in the program. One hundred twenty-one (9.8%) patients died. Mortality rates were 33.3 (95% CI, 25.5 - 43.0), 19.1 (95% CI, 14.4 - 25.2), and 2.9 (95% CI, 1.8 - 4.8) deaths/100 person-years in the pretreatment interval, during the first 4 months of ART (early deaths), and after 4 months of ART (late deaths), respectively. Pretreatment and early treatment deaths together accounted for 87% of deaths, and were independently associated with advanced immunodeficiency at enrollment. Late deaths were comparatively few and were only associated with the response to ART at 4 months. Nondeath program losses (loss to follow-up, 2.3%; transfer-out, 1.9%; relocation, 0.7%) were not associated with immune status and were evenly distributed during the study period. Conclusions. Loss to follow-up and late mortality rates were low, reflecting good cohort retention and treatment response. However, the extremely high pretreatment and early mortality rates indicate that patients are enrolling in ART programs with far too advanced immunodeficiency. Causes of late access to the ART program, such as delays in health care access, health system delays, or inappropriate treatment criteria, need to be addressed.

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Levy V, Grant RM. **Antiretroviral therapy for hepatitis B virus - HIV - Coinfected patients: Promises and pitfalls.** *Clinical Infectious Diseases* 2006;43(7):904-910.

Abstr. Coinfections with human immunodeficiency virus (HIV) and hepatitis B virus (HBV) are common globally. HIV infection modifies the course of HBV infection by increasing rates of chronicity, prolonging HBV viremia, and increasing liver-related morbidity. To minimize the emergence of HIV and/or HBV resistance, as well as the emergence of liver enzyme flares, the treatment of both infections should be coordinated. Lamivudine or emtricitabine monotherapy readily selects resistant strains in the YMDD motif of the polymerase gene. Adefovir monotherapy has moderate effectiveness in HIV-HBV-coinfected patients who have YMDD mutation. If HBV treatment can be deferred until combination antiretroviral therapy for HIV infection is needed, the combination of tenofovir plus lamivudine or emtricitabine provides potent HBV therapy and a solid backbone for HIV combination antiretroviral therapy, and it likely decreases the emergence of HBV resistance.

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Makombe S, Libamba E, Mhango E, Teck ODA, Aberle Grasse J, Hochgesang M, Schouten EJ, Harries AD. **Who is accessing antiretroviral therapy during national scale-up in Malawi?** *Transactions of the Royal Society of Tropical Medicine and Hygiene* 2006;100(10):975-979.

Abstr. Malawi is scaling-up provision of free antiretroviral therapy (ART) in the public sector. In the fourth quarter of 2004 and the first quarter of 2005, 3261 and 4530 new patients, respectively, were started on ART. Of these patients, approximately 40% were male and 95% were adults aged ≥ 13 years. The age group data show that women who accessed ART were in general 10 years younger than men. Between 84% and 90% of patients were started on ART because of being clinically assessed as being in WHO stages III or IV, with the remainder started on ART owing to a low CD4 lymphocyte count. The number of tuberculosis (TB) patients started on ART was 351 (11% of ART patients) in the fourth quarter of 2004 and 702 (15% of ART patients, and 16% of registered TB patients) in the first quarter of 2005. Twenty-nine pregnant women were referred to ART from prevention of mother-to-child transmission programmes in the first quarter of 2005. Between 56% and 62% of patients were subsistence farmers, housewives or in business. Steady progress is being made with national scale-up, although more attention needs to be directed to children, pregnant women and patients with TB to improve their access to ART.

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Manosuthi W, Chottanapand S, Thongyen S, Chaovavanich A, Sungkanuparph S. **Survival rate and risk factors of mortality among HIV/tuberculosis-coinfected patients with and without antiretroviral therapy.** *Journal of Acquired Immune Deficiency Syndromes* 2006;43(1):42-46.

Abstr. Background: The impact of antiretroviral therapy (ART) on survival among patients coinfected with HIV and tuberculosis (TB) has not been well established. Methods: A retrospective cohort study was conducted among HIV-infected patients with TB between January 2000 and December 2004. Patients were categorized into ART+ group (received ART) and ART- group (did not receive ART) and were followed until April 2005. Results: A total of 1003 patients were identified; 411 in ART+ group and 592 in ART- group. Median (interquartile range) CD4 count was 53 (20-129) cells/mm³. Survival rates at 1, 2, and 3 years after TB diagnosis were 96.1%, 94.0%, and 87.7% for ART+ group and 44.4%, 19.2%, and 9.3% for ART- group (log-rank test, P < 0.001). Cox proportional hazard model showed that ART was associated with lower mortality rate;

gastrointestinal TB and multidrug resistant TB were associated with higher mortality rate ($P < 0.05$). Among patients in ART+ group, the patients who delayed ART ≥ 6 months after TB diagnosis had a higher mortality rate than those who initiated ART < 6 months after TB diagnosis ($P 0.018$, hazard ratio = 2.651, 95% confidence interval = 1.152-6.102). Conclusions: Antiretroviral therapy substantially reduces mortality rate among HIV/TB-coinfected patients. Initiation of ART within 6 months of TB diagnosis is associated with greater survival.

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Miller CM, Gruskin S, Subramanian SV, Rajaraman D, Heymann SJ. **Orphan care in Botswana's working households: Growing responsibilities in the absence of adequate support**. American Journal of Public Health 2006;96(8):1429-1435.

Abstr. Objectives. Botswana has one of the world's highest HIV-prevalence rates and the world's highest percentages of orphaned children among its population. We assessed the ability of income-earning households in Botswana to adequately care for orphans. Methods. We used data from the Botswana Family Health Needs Study (2002), a sample of 1033 working adults with caregiving responsibilities who used public services, to assess whether households with orphan-care responsibilities encountered financial and other difficulties. Thirty-seven percent of respondents provided orphan care, usually to extended family members. We applied logistic regression models to determine the factors associated with experiencing problems related to orphan caregiving. Results. Nearly half of working households with orphan-care responsibilities reported experiencing financial and other difficulties because of orphan care. Issues of concern included caring for multiple orphans, caring for sick adults and orphans simultaneously, receiving no assistance, and low income. Conclusions. The orphan crisis is impoverishing even working households, where caregivers lack sufficient resources to provide basic needs. Neither the public sector nor communities provide adequate safety nets. International assistance is critical to build capacity within the social welfare infrastructure and to fund community-level activities that support households. Lessons from Botswana's orphan crisis can provide valuable insights to policymakers throughout sub-Saharan Africa.

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Mshana GH, Wamoyi J, Busza J, Zaba B, Changalucha J, Kaluvya S, Urassa M. **Barriers to accessing antiretroviral therapy in Kisesa, Tanzania: A qualitative study of early rural referrals to the national program**. AIDS Patient Care and Stds 2006;20(9):649-657.

Abstr. This community-based, qualitative study conducted in rural Kisesa District, Tanzania, explores perceptions and experiences of barriers to accessing the national antiretroviral programme among self-identified HIV-positive persons. Part of wider operations research around local introduction of HIV therapy, the study involved consultation with villagers and documented early referrals' progress through clinical evaluation and, if eligible, further training and drug procurement. Data collection consisted of 16 participatory group discussions with community members and 18 in-depth interviews with treatment-seekers. Although participants welcomed antiretroviral therapy, they feared that transportation and supplementary food costs, the referral hospital's reputation for being unfriendly and confusing, and difficulties in sustaining long-term treatment would limit accessibility. Fear of stigma framed all concerns, posing challenges for contacting referrals who did not want their status disclosed or expressed reluctance to identify a "treatment buddy" as required by the programme. To mitigate logistical barriers, transportation costs were paid and hospital visits facilitated. Participants reported satisfaction with eligibility testing, finding the process easier than anticipated. Most were willing to join a support group and some changed attitudes toward disclosure. However, both experienced and anticipated discrimination continue to hinder widespread antiretroviral therapy (ART) uptake. While simple measures to reduce perceived barriers improved initial access to treatment and helped overcome anxiety among early referrals, pervasive stigma remains the most formidable barrier. Encouraging successful referrals to share their positive experiences and contribute to nascent community mobilization could start to address this seemingly intractable problem.

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Nachega JB, Hislop M, Dowdy DW, Lo M, Omer SB, Regensberg L, Chaisson RE, Maartens G. **Adherence to highly active antiretroviral therapy assessed by pharmacy claims predicts survival in HIV-infected South African adults**. Journal of Acquired Immune Deficiency Syndromes 2006;43(1):78-84.

Abstr. It is unclear how adherence to highly active antiretroviral therapy (HAART) may best be monitored in large HIV programs in sub-Saharan Africa where it is being scaled up. We aimed to evaluate the association between HAART adherence, as estimated by pharmacy claims, and survival in HIV-1-infected South African adults enrolled in a private-sector AIDS management program. Of the 6288 patients who began HAART

between January 1999 and August 2004, 3 805 (61%) were female and 6094 (97%) were black African. HAART adherence was ≥ 80 for 3298 patients (52%) and 100% for 1916 patients (30%). Women were significantly more likely to have adherence $\geq 80\%$ than men (54% vs 49%, $P < 0.001$). The median (interquartile range) follow-up time was 1.8 (1.37-2.5) years. As of 1 September 2004, 222 patients had died—a crude mortality rate of 3.5%. In a multivariate Cox regression model, adherence $< 80\%$ was associated with lower survival (relative hazard 3.23; 95% confidence interval: 2.37-4.39). When medication adherence was divided into 5 strata with a width of 20% each, each stratum had lower survival rates than the adjacent, higher-adherence stratum. Among other variables tested, only baseline CD4(+) T-cell count was significantly associated with decreased survival in multivariate analysis (relative hazard 5.13; 95% confidence interval: 3.42-7.72, for CD4(+) T-cell count ≤ 50 cells/ μ L vs > 200 cells/ μ L). Pharmacy-based records may be a simple and effective population-level tool for monitoring adherence as HAART programs in Africa are scaled up.

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Nuesch R, Srasuebku P, Ananworanich J, Ruxrungtham K, Phanuphak P, Duncombe C. **Monitoring the toxicity of antiretroviral therapy in resource limited settings: a prospective clinical trial cohort in Thailand.** *Journal of Antimicrobial Chemotherapy* 2006;58(3):637-644.

Abstr. Background: One of the many challenges which come together with the implementation of antiretroviral therapy (ART) in settings with limited resources is the monitoring of toxicity. This monitoring increases costs of ART and strains resources. We therefore investigated the necessity for laboratory toxicity monitoring of ART in Thailand. Design, methods and participants: A prospective Thai cohort of 417 HIV-infected patients were enrolled in randomized clinical trials investigating ART. Time-dependent occurrence of grade III/IV abnormal laboratory values as defined by the AIDS Clinical Trial Group was analysed. Results: During a median observation period of 3.7 years (2.4-4.3) 142 grade III/IV toxicities occurred in 101 (24.2%) patients. Hepatic toxicity ($n = 33$, 7.9%), hypercholesterolaemia ($n = 57$, 13.7%), hypertriglyceridaemia ($n = 26$, 6.2%), anaemia ($n = 16$, 3.8%) and low platelet counts ($n = 8$, 1.9%) were frequently observed. Anaemia and low platelets occurred early and during the first 2 years of ART. Hepatic toxicity was seen early and throughout the observation period. Hypertriglyceridaemia and hypercholesterolaemia occurred throughout the observation period, and increased over time. Hypercreatininaemia and hyperglycaemia occurred once after 120 and 132 weeks. ART was changed or interrupted for grade III/IV hepatic toxicity, anaemia and hyperglycaemia only. The incidence rate for grade III/IV toxicity was between 5.56 (95% CI, 6.76-18.02) for low platelet counts and 41.18 (31.77-53.39) per 1000 patient years for hypercholesterolaemia. Antiretrovirals used were zidovudine, stavudine, lamivudine, zalcitabine, didanosine, efavirenz, saquinavir, ritonavir and indinavir. Conclusions: Grade III/IV toxicity is frequently observed in Thai patients treated with ART. The simple and inexpensive monitoring of ALT and haemoglobin could prevent most serious short-term toxicity. Long-term toxicity can be addressed with a yearly monitoring of triglycerides, cholesterol, glucose and creatinine if nephrotoxic drugs are used.

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Thea DM, Aldrovandi G, Kankasa C, Kasonde P, Decker WD, Semrau K, Sinkala M, Kuhn L. **Post-weaning breast milk HIV-1 viral load, blood prolactin levels and breast milk volume.** *AIDS* 2006;20(11):1539-1547.

Abstr. Background: The effect of abrupt weaning, advocated as a safe transition from exclusive breastfeeding in HIV-exposed children, on the quantity of HIV viral load in breast milk (BMVL) is not known. Objectives: To determine the effect of abrupt cessation of breastfeeding on serum prolactin, pumped breast milk volume and BMVL obtained 2 weeks after rapid weaning in HIV-infected women. Methods: Women enrolled in a prospective study (ZEBS) were randomized to abruptly wean at 20 weeks postpartum or continue exclusive breastfeeding. Breast milk was obtained at 22 weeks by electric breast pump over 10 min from 222 women who had either weaned or continued to breastfeed. Pre- and post-pumping prolactin was measured. BMVL was measured at 20 and 22 weeks in 71 randomly selected women from both groups. Results: Baseline prolactin and breast milk volume was significantly lower among women who had weaned. Detectable (68 versus 42%; $P = 0.03$) and median BMVL (448 versus < 50 copies/ml; $P = 0.005$) was significantly higher among those who had weaned in comparison with those who were still breastfeeding and was significantly higher in the same women after weaning compared with 2 weeks earlier ($P = 0.001$). Conclusions: BMVL is substantially higher after rapid weaning and this may pose an increased risk of HIV transmission if children resume breastfeeding after a period of cessation. Increases in BMVL with differing degrees of mixed feeding needs to be assessed.

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Van Geertruyden JP, Mulenga M, Mwananyanda L, Chalwe V, Moerman F, Chilengi R, Kasongo W, Van Overmeir C, Dujardin JC, Colebunders R, Kestens L, U DA. **HIV-1 immune suppression and antimalarial treatment outcome in Zambian adults with uncomplicated malaria** Journal of Infectious Diseases 2006;194(7):917-925.

Abstr. Background. Human immunodeficiency virus (HIV)-1 infected adults with low CD4 cell count have a higher risk of malaria infection and clinical malaria. We assessed the influence that HIV-1 immune suppression has on the efficacy of antimalarial treatment in adults with uncomplicated malaria Methods. This clinical trial included 971 Zambian adults with uncomplicated malaria. Patients were tested for HIV-1, and, if positive, a CD4 cell count was assessed. The primary outcome was recurrent parasitemia corrected by molecular genotyping within 45 days after treatment. Results. HIV-1 infection was detected in 33% (320/971) of adult patients with malaria. Treatment failure was not associated with HIV-1 infection (relative risk [RR], 1.12 [95% confidence interval {CI}, 0.82-1.53];). Pp. 45 HIV-1-infected patients with a CD4 cell count < 300 cells/mu L had an increased risk of recurrent parasitemia, compared with those with a CD4 cell count >= 300 cells/mu L (RR, 2.24 [95% CI, 1.20-4.14]; P = .01). After notyping, the risk of recrudescence was higher in HIV-1-infected patients with a CD4 cell count >= 300 cells/mu L than in the other patients with malaria (RR, 1.67 [95% CI, 1.13-2.47] P = .01). Conclusion. HIV-1-infected patients with malaria with a CD4 cell count < 300 cells/mu L have a higher risk of experiencing a recrudescence infection, compared with those with a CD4 cell count >= 300 cells/mu L or without HIV-1 infection.

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Wohl DA, McComsey G, Tebas P, Brown TT, Glesby MJ, Reeds D, Shikuma C, Mulligan K, Dube M, Wininger D, Huang J, Revuelta M, Currier J, Swindells S, Fichtenbaum C, Basar M, Tungsiripat M, Meyer W, Weihe J, Wanke C. **Current concepts in the diagnosis and management of metabolic complications of HIV infection and its therapy.** Clinical Infectious Diseases 2006;43(5):645-653.

Abstr. Changes in fat distribution, dyslipidemia, disordered glucose metabolism, and lactic acidosis have emerged as significant challenges to the treatment of human immunodeficiency virus (HIV) infection. Over the past decade, numerous investigations have been conducted to better define these conditions, identify risk factors associated with their development, and test potential therapeutic interventions. The lack of standardized diagnostic criteria, as well as disparate study populations and research methods, have led to conflicting data regarding the diagnosis and treatment of metabolic and body shape disorders associated with HIV infection. On the basis of a review of the medical literature published and/or data presented before April 2006, we have prepared a guide to assist the clinician in the detection and management of these complications.

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Zvandasara P, Hargrove JW, Ntozini R, Chidawanyika H, Mutasa K, Iliff PJ, Moulton LH, Mzengeza F, Malaba LC, Ward BJ, Nathoo KJ, Zijenah LS, Mbizvo M, Zunguza C, Humphrey JH. **Mortality and morbidity among postpartum HIV-positive and HIV-negative women in Zimbabwe: Risk factors, causes, and impact of single-dose postpartum vitamin A supplementation.** Journal of Acquired Immune Deficiency Syndromes 2006;43(1):107-116.

Abstr. Background: Vitamin A deficiency is common among women in resource-poor countries and is associated with greater mortality during HIV. Methods: Fourteen thousand one hundred ten mothers were tested for HIV and randomly administered 400,000 IU vitamin A or placebo at less than 96 hours postpartum. The effects of vitamin A and HIV status on mortality, health care utilization, and serum retinol were evaluated. Results: Four thousand four hundred ninety-five (31.9%) mothers tested HIV positive. Mortality at 24 months was 2.3 per 1000 person-years and 38.3 per 1000 person-years in HIV-negative and HIV-positive women, respectively. Vitamin A had no effect on mortality. Tuberculosis was the most common cause of death, and nearly all tuberculosis-associated deaths were among HIV-positive women. Among HIV-positive women, vitamin A had no effect on rates of hospitalization or overall sick clinic visits, but did reduce clinic visits for malaria, cracked and bleeding nipples, pelvic inflammatory disease, and vaginal infection. Among HIV-negative women, serum retinol was responsive to vitamin A, but low serum retinol was rare. Among HIV-positive women, serum retinol was largely unresponsive to vitamin A, and regardless of treatment group, the entire serum retinol distribution was shifted 25% less than that of HIV-negative women 6 weeks after dosing. Conclusions: Single-dose postpartum vitamin A supplementation had no effect on maternal mortality, perhaps because vitamin A status was adequate in HIV-negative women and apparently unresponsive to supplementation in HIV-positive women.

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