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Citation format (by alphabetical order of the authors): Author(s). **Title**. Source. **Abstr.** (Authors' abstract) or **Notes** (selection from the paper) **Author address**, if available, **Free full text**, if available

Calmy A, Pinoges L, Szumilin E, Zachariah R, Ford N, Ferradini L. **Generic fixed-dose combination antiretroviral treatment in resource-poor settings: multicentric observational cohort.** *AIDS* 2006;20(8):1163-1169.

Abstr. Background: The use fixed-dose combination (FDC) is a critical tool in improving HAART. Studies on the effectiveness of combined lamivudine, stavudine and neviraz pine (3TC/d4T/NVP) are scarce. Objective: To analyse 6861 patients in a large observational cohort from 21 Medecins Sans Frontieres (MSF) HIV/AIDS programmes taking 3TC/d4T/NVP, with subcohort analyses of patients at 12 and 18 months of treatment. Methods: Survival was analysed using Kaplan-Meier method and factors associated with progression to death with Cox proportional hazard ratio. Results: Median baseline CD4 cell count at initiating of FDC was 89 cells/ μ l [inter-quartile range (IQR), 33-158]. The median follow-up time was 4.1 months (IQR, 1.9-7.3). The incidence rate of death during follow-up was 14.2/100 person-years [95% confidence interval (CI), 13.8-14.5]. Estimates of survival (excluding those lost to follow-up) were 0.93 (95%CI, 92-94) at 6 months (n =2,231) and 0.90(95%CI, 8991) at 12 months (n = 472). Using a Cox model, the following factors were associated with death: male gender, symptomatic infection, body mass index < 18 kg/m² and CD4 cell count 15-50 cells/ μ l or < 15 cells/ μ l. Subcohort analysis of 655 patients after 1 year of follow-up (M] 2 FDC cohort) revealed that 77% remained on HAART, 91% of A these still on the FDC regimen; 5% discontinued the FDC because of drug intolerance. At 18 months, 77% of the patients remained on HAART. Conclusions: Positive outcomes for d4T/3TC/NVP are reported for up to 18 months in terms of efficacy and safety.

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Danel C, Moh R, Minga A, Anzian A, Ba Gomis O, Kanga C, Nzunetu G, Gabillard D, Rouet F, Sorho S, Chaix ML, Eholie S, Menan H, Sauvageot D, Bissagnene E, Salamon R, Anglaret X. **CD4-guided structured antiretroviral treatment interruption strategy in HIV-infected adults in west Africa (Trivacan ANRS 1269 trial): a randomised trial.** *Lancet* 2006;367(9527):1981-1989.

Abstr. Background Structured treatment interruptions of highly-active antiretroviral therapy (HAART) might be particularly relevant for sub-Saharan Africa, where cost-saving strategies could help to increase the number of patients on HAART. We did a randomised trial of structured treatment interruption in Abidjan, Cote d'Ivoire. Methods HIV-infected adults were randomised to receive continuous HAART (CT), CD4-guided HAART (CD4GT) with interruption and reintroduction thresholds at 350 and 250 cells per mm³, respectively, or 2-months-off, 4-months-on HAART. Primary endpoints were death and severe morbidity (any WHO stage 3 or 4 events and any events leading to death) at month 24. We report data from the CT and CD4GT groups until Oct 31, 2005, when the data safety monitoring board recommended to prematurely stop the CD4GT arm. Analyses were intention-to-treat. This study is registered at ClinicalTrials.gov, number NCT00158405. Results 326 adults (median CD4 count nadir 272 per mm³) were randomised to the CT or CD4GT groups and followed up for median of 20 months. Incidence of mortality (per 100 person-years) was not different between groups (CT 0.6, CD4GT 1.2; p=0.57). Incidence of severe morbidity (per 100 person-years) was higher in the CDG4T group (17.6) than in the CT group (6.7; p=0.001). The most frequent severe events were invasive bacterial diseases. 79% of severe morbidity episodes occurred in patients with CD4 count 200-500 per mm³. Conclusion Patients on CD4GT had severe morbidity rates 2.5-fold higher than those on CT This difference was mainly due to high rates of common diseases in patients with CD4 count 200-500 per mm³. This CD4-guided structured treatment interruption strategy should not be recommended in Abidjan.

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Deeks SG. **Antiretroviral treatment of HIV infected adults [Clinical review].** *British Medical Journal* 2006;332(7556):1489-1493.

Introduction. It has been about 10 years since the first report that three drug combination antiretroviral therapy can durably suppress HIV replication.¹ Subsequent studies have confirmed that when used appropriately highly active antiretroviral therapy (see box 1) can suppress viral replication to such low levels that the virus is unable to generate drug resistance mutations. Theoretically, once this level of viral suppression is achieved, treatment should work indefinitely, and the long term risk of morbidity and mortality related to HIV associated immunodeficiency becomes negligible. Experience to date suggests that lifelong suppression of HIV is feasible. This review is aimed at informing clinicians about the current management of HIV infection. Authoritative and continuously updated reviews are available on the web (for example, the US Department of Health and Human Services treatment guidelines at www.hivatis.org); this review does not attempt to exhaustively summarise the literature or to provide guidance to clinicians . . .

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Etard JF, Ndiaye I, Thierry Mieg M, Gueye NFN, Gueye PM, Laniece I, Dieng AB, Diouf A, Laurent C, Mboup S, Sow PS, Delaporte E. **Mortality and causes of death in adults receiving highly active antiretroviral therapy in Senegal: a 7-year cohort study.** AIDS 2006;20(8):1181-1189.

Abstr. Objectives: To evaluate survival and investigate causes of death among HIV-1 infected adults receiving HAART in Senegal. Design: An observational prospective cohort. Methods: Mortality was assessed in the first patients enrolled between August 1998 and April 2002 in the Senegalese antiretroviral drug access initiative. First-line regimen combined two nucleoside reverse transcriptase inhibitors and either a non-nucleoside reverse transcriptase inhibitor or a protease inhibitor. The most likely causes of death were ascertained through medical records or post-mortem interviews (verbal autopsy). Results: Four hundred and four patients (54.7% women) were enrolled in the study and were followed for a median of 46 months (interquartile range: 32-57 months) after HAART initiation. At baseline, 5% were antiretroviral therapy (ART) non-naïve, 39 and 55% were respectively at CDC stage B and C, median age, CD4 cell count and viral load were 37 years, 128 cells/ μ l and 5.2 log cp/ml, respectively. Ninety-three patients died during follow-up and the overall incidence rate of death was 6.3/100 person-years [95% confidence interval (CI), 5.2-7.7]. During the first year after HAART initiation, 47 patients died and seven were lost to follow-up, yielding to a probability of dying of 11.7% (95% CI, 8.9-15.3%). The death rate, which was highest during the first year after HAART initiation, decreased with time yielding a cumulative probability of dying of 17.4% (95% CI, 13.9-21.5%) and 24.6% (95% CI, 20.4-29.4%) at 2 and 5 years. Causes of death were ascertained in 76 deaths. Mycobacterial infections, neurotropic infections and septicemia were the most frequent likely causes of death. Conclusions: This study underlines the early mortality pattern after HAART initiation and highlights the leading role of mycobacterial infections in the causes of death.

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Gona P, Van Dyke RB, Williams PL, Dankner WM, Chernoff MC, Nachman SA, Seage GR. **Incidence of opportunistic and other infections in HIV-infected children in the HAART era.** JAMA 2006;296(3):292-300.

Abstr. Context Combination anti-retroviral therapy or highly active antiretroviral therapy (HAART) has resulted in a dramatic decline in the incidence of opportunistic and other infections in human immunodeficiency virus (HIV)-infected adults and children. Objectives To estimate the incidence of 29 targeted opportunistic and other infections occurring in the era of HAART-between January 1, 2001, and December 31, 2004-in HIV-infected infants, children, and adolescents followed up in Pediatric AIDS Clinical Trials Group (PACTG) 219C; to compare incidence rates in the HAART era to those of the pre-HAART era; and to test for linear trends over time in the HAART era. Design, Setting, and Participants Ongoing, multicenter, prospective cohort study designed to examine long-term outcomes in HIV-infected children. The study population included 2767 children enrolled between September 15, 2000, and December 31, 2004, with information entered in the database up to August 1, 2005, when data analysis was conducted. The pre-HAART era comparison population included 3331 children enrolled in 13 PACTG protocols from October 1988 to August 1998. Main Outcome Measures First occurrence of each of the 29 targeted infections. Results Seventy-five percent of the children were enrolled in 2000 and 2001, 90% acquired HIV perinatally, 52% were girls, and 59% were black. The median age was 8.2 years (range, 6-13 years). The median duration of follow-up was 3.4 years. Overall, 553 first episodes of a specific infection occurred among 395 (14%) of the study participants. The number of events for the 4 most common first-time infections and their incidence rates (IRs) per 100 person-years were 123 bacterial pneumonia (IR, 2.15; 95% confidence interval [CI], 1.79-2.56), 77 herpes zoster (IR, 1.11; 95% CI, 0.88-1.39), 57 dermatophyte infections (IR, 0.88; 0.67-1.14), and 52 oral candidiasis (IR, 0.93; 95% CI, 0.70-1.22). Incidence rates of first bacteremia, Pneumocystis jirovecii pneumonia, disseminated Mycobacterium avium complex, lymphoid interstitial pneumonitis, systemic fungal infection, cytomegalovirus retinitis, and tuberculosis were all less than 0.50 per 100 person-years. There were no statistically significant linear trends in incidence for any of the 29 infections over the 4 calendar years. However, infection rates were significantly lower than those reported in the PACTG in the pre-HAART era. The pre-HAART IRs were as follows: for bacterial pneumonia, IR, 11.1; 95% CI, 10.3-12.0; bacteremia, IR, 3.3; 95% CI, 2.9-3.8; herpes zoster, IR, 2.9; 95% CI, 2.6-3.3; disseminated M avium complex, IR, 1.8; 95% CI, 1.5-2.1; P jirovecii, IR, 1.3; 95% CI, 1.1-1.6; oral candidiasis, IR, 1.2; 95% CI, 1.0-1.5; cytomegalovirus retinitis, IR, 0.5; 95% CI, 0.3-0.6; and tuberculosis, IR, 0.2; 95% CI, 0.1-0.4. Conclusions Opportunistic infections and other related infections are uncommon in children in the HAART era, and infection rates continue to be lower than those reported in the pre-HAART era. Continued surveillance is important to assess the long-term effect of HAART on the occurrence of opportunistic and other related infections in children.

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Kali PBN, Gray GE, Violari A, Chaisson RE, McIntyre JA, Martinson NA. **Combining PMTCT with active case finding for tuberculosis**. *Journal of Acquired Immune Deficiency Syndromes* 2006;42(3):379-381.

Abstr. Tuberculosis (TB) is the preeminent manifestation of HIV infection and has become a leading cause of maternal mortality and morbidity in high HIV prevalence settings. Active TB in pregnant women has potentially serious consequences for fetuses and newborns. In Soweto, South Africa, there is a more than 90% uptake of voluntary counseling and HIV testing during routine antenatal care, and almost one third of pregnant women are HIV-infected. The posttest counseling session of the prevention of mother-to-child transmission program provides an opportunity to screen HIV-infected pregnant women for TB. In this Study, 370 HIV-infected pregnant women were screened for symptoms of active TB by lay counselors at the posttest counseling session. If symptomatic, they were referred to nurses who investigated them further. Eight women were found to have previously undiagnosed, smear-negative, culture-confirmed TB (2160/100 000). The mean CD4 count in those with active TB compared to those without TB was 276 x 10(6) cells per liter vs 447 x 10(6) cells per liter (P = 0.051). Symptoms most associated with active TB were hemoptysis and fever. We conclude that rates of TB in HIV-infected pregnant women are high, and screening for TB during routine antenatal care should be implemented in high HIV prevalence settings.

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Manosuthi W, Sungkanuparph S, Thakkinstian A, Rattanasiri S, Chaovavanich A, Prasithsirikul W, LikAnonsakul S, Ruxrungtham K. **Plasma nevirapine levels and 24-week efficacy in HIV-infected patients receiving nevirapine-based highly active antiretroviral therapy with or without rifampicin**. *Clinical Infectious Diseases* 2006;43(2):253-255.

Abstr. Seventy human immunodeficiency virus (HIV)-infected patients receiving rifampicin and 70 HIV-infected patients not receiving rifampicin were enrolled to receive 400 mg of nevirapine-based highly active antiretroviral therapy per day. Mean plasma nevirapine levels at 8 and 12 weeks were lower in patients receiving rifampicin (P = .048). However, virological and immunological outcomes at 24 weeks were not different between the 2 groups (P > .05).

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Vermund SH. **Millions of life-years saved with potent antiretroviral drugs in the United States: A celebration, with challenges [Editorial commentary]**. *Journal of Infectious Diseases* 2006;194(1):1-5.

Abstr. In this issue of the *Journal*, Walensky et al. estimate the benefits that have been gained from multidrug antiretroviral therapies (ARTs) since 1989. Their finding of 3 million years of life saved in the United States quantifies ART benefits at the population level, complementing the well-known data on plummeting US death rates and lower AIDS case report rates noted in the era of potent therapy. The authors' detailed sensitivity analyses, varying key estimated parameters in their models, indicate that less-conservative assumptions generate an estimate of >5 million years of life saved, a plausible "higher-end" estimate of benefit. The typical HIV-infected person now receiving potent combination ART lives at least 13–14 years longer than if he or she were to forego this therapy or if it were otherwise unavailable. Quantifying the survival benefits of expanded diagnosis and modern care suggests that the economic and humanitarian benefits are greater than were hitherto appreciated.

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Walensky RP, Paltiel AD, Losina E, Mercincavage LM, Schackman BR, Sax PE, Weinstein MC, Freedberg KA. **The survival benefits of AIDS treatment in the United States**. *Journal of Infectious Diseases* 2006;194(1):11-19.

Abstr. Background. As widespread adoption of potent combination antiretroviral therapy (ART) reaches its tenth year, our objective was to quantify the cumulative survival benefits of acquired immunodeficiency syndrome (AIDS) care in the United States. Methods. We defined eras corresponding to advances in standards of human immunodeficiency virus (HIV) disease care, including opportunistic infection prophylaxis, treatment with ART, and the prevention of mother-to-child transmission (pMTCT) of HIV. Per-person survival benefits for each era were determined using a mathematical simulation model. Published estimates provided the number of adult patients with new diagnoses of AIDS who were receiving care in the United States from 1989 to 2003. Results. Compared with survival associated with untreated HIV disease, per-person survival increased 0.26 years with *Pneumocystis jirovecii* pneumonia prophylaxis alone. Four eras of increasingly effective ART in addition to prophylaxis resulted in per-person survival increases of 7.81, 11.05, 11.57, and 13.33 years, compared with the absence of treatment. Treatment for patients with AIDS in care in the United States since 1989 yielded a total survival benefit of 2.8 million years. pMTCT averted nearly 2900 infant infections, equivalent to 137,000

additional years of survival benefit. Conclusions. At least 3.0 million years of life have been saved in the United States as a direct result of care of patients with AIDS, highlighting the significant advances made in HIV disease treatment.

See the editorial commentary by Vermund.

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Watera C, Todd J, Muwonge R, Whitworth J, Nakiyingi Miiro J, Brink A, Miiro G, Antvelink L, Kamali A, French N, Mermin J. **Feasibility and effectiveness of cotrimoxazole prophylaxis for HIV-1-infected adults attending an HIV/AIDS clinic in Uganda.** Journal of Acquired Immune Deficiency Syndromes 2006;42(3):373-378.

Abstr. Background: Cotrimoxazole is recommended for prevention of opportunistic infections in symptomatic HIV patients in sub-Saharan Africa. Methods: We examined the feasibility and effectiveness of daily cotrimoxazole prophylaxis in a well-established cohort of HIV-infected adults attending clinics in Entebbe, Uganda. We compared mortality and morbidity rates for 12 months before and after the introduction of cotrimoxazole. Results: Between August 2000 and February 2002, 94% of cohort members were enrolled onto cotrimoxazole prophylaxis. Revisits were scheduled every 4 weeks to replenish pills; patients attended 61% of revisits. The main reasons for nonenrollment and defaulting were lack of transport, being away from home, and sickness. Drug-related adverse events, mainly itching and rash, were seen in 4% of participants. Although bacterial resistance rate to cotrimoxazole was high, the adjusted mortality incidence rate ratio was significantly reduced after the introduction of cotrimoxazole (0.76; 95% confidence interval, 0.60-0.96; P = 0.020). Overall febrile events and morbidity rates were unchanged after the introduction of cotrimoxazole, but the incidence of malaria was reduced (incidence rate ratio, 0.31; 95% confidence interval, 0.13-0.72). Conclusions: Cotrimoxazole prophylaxis can be introduced into routine HIV clinic activities and is associated with a reduction in overall mortality and malaria morbidity, even in all area with high bacterial resistance. These results reinforce the need for large-scale provision of cotrimoxazole prophylaxis for all HIV-positive patients in developing countries.

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