HIV Care & PMTCT in Resource-Limited Settings

Monthly Intelligence Report

Back Issues on Line

prepared by the Bordeaux Working Group

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Citation format (by alphabetical order of the authors): Author(s). Title. Source. Abstr. (Authors’ text) or Introduction (Authors’ text) or Selection (Selected sections of the paper) or Notes or Abstr. Edited (Written by the Bordeaux Working Group). Author Address, if available, Free Full Text, if available
Andia I, Kaida A, Maier M, Guzman D, Emenyonu N, Pepper L, Bangsberg DR, Hogg RS. 

Abstr. Objectives. We investigated whether the prevalence of contraceptive use among women who are HIV positive varied according to use of highly active antiretroviral therapy (HAART) in Mbarara, Uganda. Methods. We used data from a cross-sectional survey of 484 women who were HIV positive (18-50 years) and were attending Mbarara University’s HIV clinic, 45% of whom were receiving HAART. Multivariate logistic regression was used to investigate the association between HAART use and contraceptive use. Data were collected between November 2005 and June 2006. Results. Overall, 45% of the women were sexually active in the previous 3 months. Of these, 85% reported using contraceptive methods, with 84% reporting use of barrier contraceptive methods. Women receiving HAART were more than twice as likely to use contraceptive methods (adjusted odds ratio [AOR]=2.64; 95% confidence interval [CI]=1.07, 6.49) and more than 3 times as likely to use barrier contraceptive methods (AOR=3.62; 95% CI=1.54, 8.55) than were women not receiving HAART. Conclusions. Our findings support the need for increased attention to better integration of reproductive health and HIV and AIDS services for women who are HIV positive.

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Abstr. BACKGROUND: Maternal CD4 count predicts child mortality in HIV-uninfected children born to HIV-infected women. METHODS: To explore the mediating role of breastfeeding cessation in this relationship, we compared marginal structural models of maternal CD4 count on child death with and without adjustment for breastfeeding. RESULTS: In crude analyses, children of mothers with CD4 < 200 during pregnancy were 3.2 times more likely to die by 18 months (CI 1.3-8.1) as children whose mothers had CD4 > 500. Earlier breastfeeding cessation was also associated with low CD4 (HR 1.8; CI 1.2-2.7). After adjusting for breastfeeding and low birth weight using a marginal structural model, the low CD4 count-child mortality association through 18 months was reduced 17%. The change was overestimated using a traditional Cox proportional hazards model (35% reduction in HR from 3.4 to 2.5). CONCLUSIONS: Our analysis suggests that only a small part of the effect of low vs high CD4 count on child mortality through 18 months is mediated through breastfeeding cessation. Our results must be taken into account when deciding whether or not to recommend breastfeeding for infants of HIV-infected mothers.

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Garnett GP, Baggaley RF. Treating our way out of the HIV pandemic: could we, would we, should we? Lancet 2009;373(9657):9-11.

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Abstr. BACKGROUND: Roughly 3 million people worldwide were receiving antiretroviral therapy (ART) at the end of 2007, but an estimated 6.7 million were still in need of treatment and a further 2.7 million became infected with HIV in 2007. Prevention efforts might reduce HIV incidence but are unlikely to eliminate this disease. We investigated a theoretical strategy of universal voluntary HIV testing and immediate treatment with ART, and examined the conditions under which the HIV epidemic could be driven towards elimination. METHODS: We used mathematical models to explore the effect on the case reproduction number (stochastic model) and long-term dynamics of the HIV epidemic (deterministic transmission model) of testing all people in our test-case community (aged 15 years and older) for HIV every year and starting people on ART immediately after they are diagnosed HIV positive. We used data from South Africa as the test case for a generalised epidemic, and assumed that all HIV transmission was heterosexual. FINDINGS: The studied strategy could greatly accelerate the transition from the present endemic phase, in which most adults living with HIV are not receiving ART, to an elimination phase, in which most are on ART, within 5 years. It could reduce HIV incidence and mortality to less than one case per 1000 people per year by 2016, or within 10 years of full implementation of the strategy, and reduce the prevalence of HIV to less than 1% within 50 years. We estimate that in 2032, the yearly cost of the present strategy and the theoretical strategy would both be US$1.7 billion; however, after this time, the cost of the present strategy would continue to increase whereas that of the theoretical strategy would decrease. INTERPRETATION: Universal voluntary HIV testing and immediate ART, combined with present prevention approaches, could have a major effect on severe generalised HIV/AIDS epidemics. This approach merits further mathematical modelling, research, and broad consultation. FUNDING: None.

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Abstr. BACKGROUND: Antiretroviral therapy (ART) may influence the biological, social and behavioral determinants of pregnancy in HIV-infected women. However, there are limited longitudinal data on the reproductive intentions and outcomes among women on ART in Africa. METHODOLOGY /PRINCIPAL FINDINGS: Using a prospective cohort design, we analyzed trends in desire for children and predictors of pregnancy among a cohort of 733 HIV-infected women in rural Uganda who initiated ART between May 2003 and May 2004 and were followed up in their homes until June 2006. Women answered in-depth social and behavioral questionnaires administered every quarter in year 1 after initiating ART, and every 6 to 12 months thereafter. Use of family planning methods was assessed at 18 and 24 months after starting ART. We tested for non-constant pregnancy incidence by using a shape parameter test from the Weibull distribution. We modeled repeated measurements of all variables related to the women's desire for children over time using a generalized estimating equation (GEE) extension to the logistic regression model. Risk factors for pregnancy were examined using Cox proportional hazards model. 711 women eligible for the study were followed-up for a median time of 2.4 years after starting ART. During this time, less than 7% of women reported wanting more children at any time point yet 120 (16.9%) women experienced 140 pregnancies and pregnancy incidence increased from 3.46 per 100 women-years (WY) in the first quarter to 9.5 per 100 WY at 24 months (p<0.0001). This was paralleled by an increase in the proportion of women...
reporting sexual activity in the past 3 months, from 24.4% at baseline to 32.5% over 24 months of follow-up (p = 0.001). Only 14% of women used permanent or semi-permanent family planning methods by their second year on ART. In the multivariate model, younger age (HR = 2.71 per 10-year decrease, 95% CI: 2.95-3.78), having a BMI>18.5 (HR = 1.09, CI: 1.01-1.18) and not having used condoms consistently in the last 3 months (HR = 1.79, CI: 1.02-3.13) were independently associated with pregnancy.

CONCLUSION/SIGNIFICANCE: Women on ART and their partners should be consistently counseled on the effects of ART in restoring fertility, and offered regularly free and comprehensive family planning services as part of their standard package of care.

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**Abstr.** BACKGROUND: Data comparing survival of formula-fed to breast-fed infants in programmatic settings are limited. We compared mortality and HIV-free of breast and formula-fed infants born to HIV-positive mothers in a program in rural, Rakai District Uganda. METHODOLOGY/PRINCIPAL FINDINGS: One hundred eighty two infants born to HIV-positive mothers were followed at one, six and twelve months postpartum. Mothers were given infant-feeding counseling and allowed to make informed choices as to whether to formula-feed or breast-feed. Eligible mothers and infants received antiretroviral therapy (ART) if indicated. Mothers and their newborns received prophylaxis for prevention of mother-to-child HIV transmission (pMTCT) if they were not receiving ART. Infant HIV infection was detected by PCR (Roche Amplicor 1.5) during the follow-up visits. Kaplan Meier time-to-event methods were used to compare mortality and HIV-free survival. The adjusted hazard ratio (Adjusted HR) of infant HIV-free survival was estimated by Cox regression. Seventy-five infants (41%) were formula-fed while 107 (59%) were breast-fed. Exclusive breast-feeding was practiced by only 25% of breastfeeding women at one month postpartum. The cumulative 12-month probability of infant mortality was 18% (95% CI = 11%-29%) among the formula-fed compared to 3% (95% CI = 1%-9%) among the breast-fed infants (unadjusted hazard ratio (HR) = 6.1(95% CI = 1.7-21.4, P-value<0.01). There were no statistically significant differentials in HIV-free survival by feeding choice (86% in the formula-fed compared to 96% in breast-fed group (Adjusted RH = 2.8[95%CI = 0.67-11.7, P-value = 0.16] CONCLUSIONS/SIGNIFICANCE: Formula-feeding was associated with a higher risk of infant mortality than breastfeeding in this rural population. Our findings suggest that formula-feeding should be discouraged in similar African settings.

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**Abstr.** OBJECTIVE:: To determine the relationship between mortality risk and the CD4 cell response to antiretroviral therapy (ART). DESIGN:: Observational community-based ART cohort in South Africa. METHODS:: CD4 cell counts were measured 4 monthly, and deaths were prospectively ascertained. Cumulative person-time accrued within a range of updated CD4 cell count strata (CD4 cell-strata) was calculated and used to derive CD4
cell-stratified mortality rates. RESULTS:: Patients (2423) (median baseline CD4 cell count of 105 cells/mul) were observed for up to 5 years of ART. One hundred and ninety-seven patients died during 3155 person-years of observation. In multivariate analysis, mortality rate ratios associated with 0-49, 50-99, 100-199, 200-299, 300-399, 400-499 and at least 500 cells/mul updated CD4 cell-strata were 11.6, 4.9, 2.6, 1.7, 1.5, 1.4 and 1.0, respectively. Analysis of CD4 cell count recovery permitted calculations of person-time accrued within these CD4 cell-strata. Despite rapid immune recovery, high mortality in the first year of ART was related to the large proportion of person-time accrued within CD4 cell-strata less than 200 cells/mul. Moreover, patients with baseline CD4 cell counts less than 100 cells/mul had much higher cumulative mortality estimates at 1 and 4 years (11.6 and 16.7%) compared with those of patients with baseline counts of at least 100 cells/mul (5.2 and 9.5%) largely because of greater cumulative person-time at CD4 cell counts less than 200 cells/mul. CONCLUSION:: Updated CD4 cell counts are the variable most strongly associated with mortality risk during ART. High cumulative mortality risk is associated with person-time accrued at low CD4 cell counts. National HIV programmes in resource-limited settings should be designed to minimize the time patients spend with CD4 cell counts less than 200 cells/mul both before and during ART. Address: The Desmond Tutu HIV Centre, Institute for Infectious Disease and Molecular Medicine, University of Cape Town, South Africa. stevelawn@yahoo.co.uk


Abstr. OBJECTIVE:: HIV counseling and testing (HCT) is a key intervention for HIV/AIDS control, and new strategies have been developed for expanding coverage in developing countries. We compared costs and outcomes of four HCT strategies in Uganda. DESIGN:: A retrospective cohort of 84 323 individuals received HCT at one of four Ugandan HCT programs between June 2003 and September 2005. HCT strategies assessed were stand-alone HCT; hospital-based HCT; household-member HCT; and door-to-door HCT. METHODS:: We collected data on client volume, demographics, prior testing and HIV diagnosis from project monitoring systems, and cost data from project accounts and personnel interviews. Strategies were compared in terms of costs and effectiveness at reaching key population groups. RESULTS:: Household-member and door-to-door HCT strategies reached the largest proportion of previously untested individuals (>90% of all clients). Hospital-based HCT diagnosed the greatest proportion of HIV-infected individuals (27% prevalence), followed by stand-alone HCT (19%). Household-member HCT identified the highest percentage of discordant couples; however, this was a small fraction of total clients (4%). Costs per client (2007 USD) were $19.26 for stand-alone HCT, $11.68 for hospital-based HCT, $13.85 for household-member HCT, and $8.29 for door-to-door HCT. CONCLUSION:: All testing strategies had relatively low per client costs. Hospital-based HCT most readily identified HIV-infected individuals eligible for treatment, whereas home-based strategies more efficiently reached populations with low rates of prior testing and HIV-infected people with higher CD4 cell counts. Multiple HCT strategies with different costs and efficiencies can be used to meet the UNAIDS/WHO call for universal HCT access by 2010. Address: US Centers for Disease Control and Prevention, National Center for HIV, Viral Hepatitis, STD, and TB Prevention, Atlanta, Georgia, USA. nmenzies@fas.harvard.edu

Abstr. BACKGROUND: Daily nevirapine (NVP) prophylaxis to HIV-exposed infants significantly reduces breast-milk HIV transmission. We assessed NVP-resistance in Indian infants enrolled in the "six-week extended-dose nevirapine" (SWEN) trial who received single-dose NVP (SD-NVP) or SWEN for prevention of breast-milk HIV transmission but who also acquired subtype C HIV infection during the first year of life. METHODS/FINDINGS: Standard population sequencing and cloning for viral subpopulations present at > or =5% frequency were used to determine HIV genotypes from 94% of the 79 infected Indian infants studied. Timing of infection was defined based on when an infant's blood sample first tested positive for HIV DNA. SWEN-exposed infants diagnosed with HIV by six weeks of age had a significantly higher prevalence of NVP-resistance than those who received SD-NVP, by both standard population sequencing (92% of 12 vs. 38% of 29; p = 0.002) and low frequency clonal analysis (92% of 12 vs. 59% of 29; p = 0.06). Likelihood of infection with NVP-resistant HIV through breast-milk among infants infected after age six weeks was substantial, but prevalence of NVP-resistance did not differ among SWEN or SD-NVP exposed infants by standard population sequencing (15% of 13 vs. 15% of 20; p = 1.00) and clonal analysis (31% of 13 vs. 40% of 20; p = 0.72). Types of NVP-resistance mutations and patterns of persistence at one year of age were similar between the two groups. NVP-resistance mutations did differ by timing of HIV infection; the Y181C variant was predominant among infants diagnosed in the first six weeks of life, compared to Y188C/H during late breast-milk transmission. CONCLUSIONS/SIGNIFICANCE: Use of SWEN to prevent breast-milk HIV transmission carries a high likelihood of resistance if infection occurs in the first six weeks of life. Moreover, there was a continued risk of transmission of NVP-resistant HIV through breastfeeding during the first year of life, but did not differ between SD-NVP and SWEN groups. As with SD-NVP, the value of preventing HIV infection in a large number of infants should be considered alongside the high risk of resistance associated with extended NVP prophylaxis. TRIAL REGISTRATION: ClinicalTrials.gov NCT00061321.

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Abstr. The transmission of HIV via breastmilk has led to various recommendations for HIV-infected mothers. In this study, the feeding practices of HIV-infected mothers in the first six months of their infants' lives were evaluated. In total, 103 consecutive mothers of children, aged 6-24 months, were evaluated for their feeding practices in the first six months of their infants' lives. The mothers were recruited in two cohorts based on their entry (PMTCT cohort) or non-entry (non-PMTCT cohort) to an HIV MTCT-prevention programme. Information obtained included maternal age, socioeconomic class, and the educational level attained. All the babies in the non-PMTCT cohort were breastfed compared to none in the PMTCT cohort. Infant formula was inadequately prepared for 77.42% of babies in the non-PMTCT cohort compared to 18.64% in the PMTCT cohort. The mixed-feeding rate was high (70.45%) in the non-PMTCT cohort. Over 70% of babies in both the cohorts were bottle-fed. Voluntary counselling and testing services in the healthcare system should be strengthened. All mothers should receive infant-feeding...
counselling, with exclusive breastfeeding being encouraged in those with unknown HIV status.

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**Abstr.** The aim of this meta-analysis study was to evaluate the relative risk of death or AIDS-defining events associated to CD4+ guided treatment interruption in patients with chronic HIV infection. A search was conducted using PubMed and Cochrane Library; key words for PubMed were: "antiretroviral therapy and interrupt*" in the full papers from January 1, 2000 up to and including December 31, 2007. To limit the publication bias, clinical trials performed on the topic of the meta-analysis were searched also on http://www.clinicaltrial.gov. Inclusion criteria of studies were: starting a CD4+ guided interruption of HAART in HIV chronically infected patients with CD4+ cell count > 350 cells/mm3, age > 13 years old, and absence of concomitant use of immunomodulatory drugs. Using a conservative approach, to be included in the meta-analysis, studies had to have a follow up period > 100 person years to minimize the bias of a too short observation time. The studies were classified into two categories: randomized clinical trial (one arm stops therapy and other arms continue HAART) and cohort studies. For each study measures of effect (hazard ratio or incidence rate ratio) were reported, when available, uncorrected and corrected for potential confounders. Publication bias was assessed graphically through funnel plot. Pooled relative risk and pooled risk difference were calculated by use of a random effects model following the DerSimonian-Laird method. Observational studies were considered separately and the incidence of primary endpoint was evaluated in each study and the cumulative incidence was calculated. Of the 555 full papers found, all abstracts were screened and 58 full text articles for potential inclusion were retrieved and 18 were retained (seven randomized clinical trials and 11 observational studies). In randomized clinical trials, the meta-analysis showed that the pooled relative risk of AIDS-defining event or mortality was 2.50 (95% CI: 1.87-3.34; p < 0.001); the pooled risk difference of AIDS-defining event or mortality was 0.02 (95% CI: capital ER, Cyrillic0.01-0.05; p = 0.168). The respective values corrected for latest CD4+ value were 1.77 (95% CI: 1.29-2.42; p < 0.001) and 0.01 (95% CI: capital ER, Cyrillic0.01-0.02; p = 0.37). The pooled relative risk of death was 1.8 (95% CI: 1.18-2.77; p = 0.007), and the corresponding pooled risk difference was 0.01 (95% CI: 0.001-0.012; p = 0.03). The risk of death resulted to have increased in patients that interrupted treatment; the corresponding value of risk difference was significant, although it was low (one extra death per 100 person years). Considering that a separate analysis corrected for the latest CD4+ value was not feasible for this endpoint, and that mortality rates in HIV-infected patients are inversely correlated with the CD4+ count, the value reported is extremely conservative. In cohort studies, the cumulative incidence of deaths or AIDS-defining events in the five studies with follow-up > 100 person years, was 0.77 (95% CI: 0.37-1.42 events per 100 person years), ranging in different studies from 0 to 3.2 events per 100 person years. This meta-analysis suggests that in patients undergoing a treatment interruption, there is an increased risk of developing AIDS or death, and that this risk is decreased if a relatively high CD4+ threshold is chosen to reinstate the treatment, while the risk difference does not reach statistical significance.

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Abstr. Risk factors for mother-to-child transmission (MTCT) of human immunodeficiency virus (HIV) via breast-feeding were evaluated in a randomized trial. HIV-infected women and their infants received zidovudine as well as single-dose nevirapine or placebo. Infants were randomized to formula-feed (FF) or breast-feed (BF) in combination with zidovudine prophylaxis. Of 1116 at-risk infants, 6 (1.1%) in the FF group and 7 (1.3%) in the BF group were infected between birth and 1 month ([Formula: see text]). Maternal receipt of nevirapine did not predict early MTCT in the BF group ([Formula: see text]). Of 547 infants in the BF group at risk for late MTCT, 24 (4.4%) were infected. Maternal HIV-1 RNA levels in plasma ([Formula: see text]) and breast milk ([Formula: see text]) predicted late MTCT. These findings support the safety of 1 month of breast-feeding in combination with maternal and infant antiretroviral prophylaxis. Trial registration. @nbsp;ClinicalTrials.gov identifiers: NCT00197691 and NCT00197652 .

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Notes. AIDS 2008;22 Suppl 4, special issue on Vulnerability of young women and girls to HIV infection in Southern Africa.

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Abstr. BACKGROUND: The President's Emergency Plan for AIDS Relief committed $15 billion to addressing HIV in resource-poor settings. OBJECTIVE: To assess the impact of The President's Emergency Plan for AIDS Relief on the treatment services of an HIV care program. DESIGN, SETTING, AND PATIENTS: Cohort study utilizing computerized medical records of nonpregnant adults enrolled into the Academic Model for the Prevention and Treatment of HIV/AIDS system, in western Kenya between 27 November 2001 and 24 July 2006. MAIN OUTCOMES MEASURES: Number of clinics and patients enrolled in Academic Model for the Prevention and Treatment of HIV/AIDS, as well as patient demographics, immunologic, and clinical characteristics during three periods defined by the availability of combination antiretroviral therapy (cART). RESULTS: Enrollment as of May 2006 was 23,539. Mean monthly enrollment increased from 64 to
815 between periods 1 and 3. The median CD4 cell count at enrollment during period 3 (172 cells/microl) was significantly higher than for period 2 (119 cells/microl; P < 0.001). World Health Organization stage at enrollment differed significantly between periods with 6.7% having stage 4 disease in period 3 compared with 13.8% during period 1 (P < 0.001). Significantly more patients had complete documentation of cART eligibility, during period 3 as compared with the previous periods. Time from enrollment to cART initiation decreased from a median of 64 weeks in period 1 to 12 weeks during period 3 (P < 0.001). CONCLUSION: The President's Emergency Plan for AIDS Relief funding has allowed Academic Model for the Prevention and Treatment of HIV/AIDS to significantly increase the number of individuals receiving HIV care and provided the ability to expand services allowing for identification of patients earlier in their disease process.

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