HIV Care & PMTCT in Resource-Limited Settings

Monthly Intelligence Report
2010, Vol 6, Issue 5

Back Issues on Line

prepared by the Bordeaux Working Group

Members: Elise Arrivé, Renaud Becquet, Mathias Bruyand, François Dabis (Chair), Antoine Jaquet, Valérie Leroy, Charlotte Lewden, Evelyne Mouillet (Coordinator), Camille Ndondoki, Joanna Orne-Gliemann (Coordinator), Freddy Perez, Hapsatou Touré.

Number of citations selected for this issue: 13

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
Discordance between CD4 cell count and CD4 cell percentage: implications for when to start antiretroviral therapy in HIV-1 infected children HIV Paediatric Prognostic Markers Collaborative Study. AIDS 2010;24(8):1213-1217.

Objective: Antiretroviral therapy (ART) guidelines for HIV-1-infected children specify both absolute CD4 cell count and CD4 percentage thresholds at which consideration should be given to initiating ART. This leads to clinical dilemma when one marker is below the threshold, whereas the other is above. Data: Were obtained on a large group of children followed longitudinally in trials and cohort studies in Europe and the USA. Follow-up was censored 6 months after the start of any antiretroviral drug other than zidovudine monotherapy. Methods: Discordance between CD4 cell count and percentage was defined in relation to ART initiation thresholds in World Health Organization (WHO) and European paediatric treatment guidelines. The relative prognostic value of CD4 cell count and percentage for progression to AIDS/death was investigated using time-updated Cox proportional hazards models, stratified by age. Results: Among 3345 children, with a total of 21 815 pairs of CD4 measurements analysed, 980 developed AIDS and/or died after a median follow-up of 1.7 years. Over one-half of children had discordant values of CD4 cell markers at the first visit when one or both treatment thresholds were crossed and approximately one-third had the same pattern of discordance at a subsequent measurement. Conclusions: More emphasis should be placed on CD4 cell count than on CD4 percentage in deciding when to start ART in HIV-1-infected children.


Background: Botswana has the most comprehensive public program in Africa for providing antiretroviral therapy to treat HIV and prevent mother-to-child transmission (PMTCT). Botswana guidelines prioritize CD4(+) cell count testing during pregnancy and initiation of highly active antiretroviral treatment (HAART) for women who qualify for treatment. We analyzed rates of HIV testing, CD4(+) cell count testing, and HAART initiation during pregnancy. Methods: From October 2007 through June 2008, we reviewed obstetric and laboratory records of women at Princess Marina Hospital in Gaborone, Botswana. Results: We recorded information from 3056 women. Of 2675 women eligible for the PMTCT program, 2623 (98%) had a documented HIV status, of whom 793 (30%) were HIV infected. Among women who were treatment naive at pregnancy conception, 397 (59%) had recorded CD4(+) cell counts, of whom 62 (16%) had a CD4(+) cell count <200 cells per cubic millimeter. Among this subset, 23 (37%) initiated HAART during pregnancy, 26 (42%) received zidovudine prophylaxis, and 13 (21%) received no therapy. Conclusions: We observed low rates of CD4(+) cell count testing and HAART initiation during pregnancy. Antenatal clinics should prioritize CD4(+) cell count testing and referral of women who qualify for HAART to maximize benefits of maternal treatment and PMTCT.


Background: In July 2007, amid some controversy over cost, Zambia was the first African country to introduce tenofovir (TDF) as a component of first-line antiretroviral therapy (ART) on a wide scale. Methods: We compared drug substitutions, mortality, and "programmatic failure" among adults starting TDF-, zidovudine (ZDV)-, and stavudine (d4T)-containing ART. Programmatic failure was defined as death, withdrawal, or loss to follow-up. Results: Between July 2007 and January 2009, 10,485 adults initiated ART (66% on TDF, 23% on ZDV, 11% on d4T), with a median follow-up time of 239 (interquartile range 98, 385) days. Those starting TDF were more likely to be male and more likely
to have indicators of severe disease at baseline. In adjusted Cox proportional hazards models, ZDV-
(adjusted hazard ratio [AHR] = 2.74, 95% confidence interval [CI] = 2.30-3.28) and d4T-based
regimens (AHR = 1.92, 95% CI = 1.55-2.38) were associated with higher risk for drug substitution
when compared with TDF-based regimens. Similar hazards were noted for overall mortality (ZDV:
AHR = 0.81, 95% CI = 0.62-1.06; d4T: AHR = 1.03, 95% CI = 0.74-1.43) and programmatic failure
(ZDV: AHR = 0.99, 95% CI = 0.88-1.11; d4T: AHR = 1.11, 95% CI = 0.96-1.28) when compared with
TDF. Conclusions: TDF is associated with similar clinical and programmatic outcomes as ZDV and
d4T but appears to be better tolerated. Although further evaluation is needed, these results are
encouraging and support Zambia's policy decision.

Address: Chi, Bh, Plot 1275 Lubutu Rd,Pob 34681, Lusaka, Zambia. bchi@uab.edu

Fox, MP, Rosen S. Patient retention in antiretroviral therapy programs up to three years on
treatment in sub-Saharan Africa, 2007-2009: systematic review. Tropical Medicine & International

Abstr. Objectives To estimate the proportion of all-cause adult patient attrition from antiretroviral
therapy (ART) programs in service delivery settings in sub-Saharan Africa through 36 months on
treatment. Methods We identified cohorts within Ovid Medline, ISI Web of Knowledge, Cochrane
Database of Systematic Reviews and four conference abstract archives. We summarized retention
rates from studies describing observational cohorts from sub-Saharan Africa reporting on adult HIV-
infected patients initiating first-line three-drug ART. We estimated all-cause attrition rates for 6, 12, 18,
24, or 36 months after ART initiation including patients who died or were lost to follow-up (as defined
by the author), but excluding transferred patients. Results We analysed 33 sources describing 39
cohorts and 226 307 patients. Patients were more likely to be female (median 65%) and had a median
age at initiation of 37 (range 34-40). Median starting CD4 count was 109 cells/mm3. Loss to follow-up
was the most common cause of attrition (59%), followed by death (41%). Median attrition at 12, 24 and
36 months was 22.6% (range 7%-45%), 25% (range 11%-32%) and 29.5% (range 13%-36.1%)
respectively. After pooling data in a random-effects meta-analysis, retention declined from 86.1% at 6
months to 80.2% at 12 months, 76.8% at 24 months and 72.3% at 36 months. Adjusting for variable
follow-up time in a sensitivity analysis, 24 month retention was 70.0% (range: 66.7%-73.3%), while 36
month retention was 64.6% (range: 57.5%-72.1%). Conclusions Our findings document the difficulties
in retaining patients in care for lifelong treatment, and the progress being made in raising overall
retention rates.

Notes: In TMIH special issue TMIH "Retention of patients in HIV/AIDS care and treatment programs in
sub-Saharan Africa", Part I: "Rates of Retention and Reasons for Attrition".

Address: Fox, Mp, Boston Univ, Ctr Global Hlth & Dev, 801 Massachusetts Ave,Crosstown 3rd Floor,
Boston, MA 02118 USA. mfox@bu.edu

Harries AD, Zachariah R, Lawn SD, Rosen S. Strategies to improve patient retention on
antiretroviral therapy in sub-Saharan Africa. Tropical Medicine & International Health 2010;15:70-75.

Abstr. The scale-up of antiretroviral therapy (ART) has been one of the success stories of sub-
Saharan Africa, where coverage has increased from about 2% in 2003 to more than 40% 5 years later.
However, tempering this success is a growing concern about patient retention (the proportion of
patients who are alive and remaining on ART in the health system). Based on the personal experience
of the authors, 10 key interventions are presented and discussed that might help to improve patient
retention. These are (1) the need for simple and standardized monitoring systems to track what is
happening, (2) reliable ascertainment of true outcomes of patients lost to follow-up, (3) implementation
of measures to reduce early mortality in patients both before and during ART, (4) ensuring
uninterrupted drug supplies, (5) consideration of simple, non-toxic ART regimens, (6) decentralization
of ART care to health centres and the community, (7) a reduction in indirect costs for patients
particularly in relation to transport to and from clinics, (8) strengthening links within and between health
services and the community, (9) the use of ART clinics to deliver other beneficial patient or family-
orientated packages of care such as insecticide-treated bed nets, and (10) innovative (thinking 'out of
the box') interventions. High levels of retention on ART are vital for individual patients, for credibility of
programmes and for on-going resource and financial support.

**Abstr.** Background: Limited information exists about effects of different highly active antiretroviral therapy (HAART) regimens and duration of regimens on mother-to-child transmission (MTCT) of HIV among women in Africa who start treatment for advanced immunosuppression. Methods: Between January 2004 to August 2008, 1142 women were followed at antenatal antiretroviral clinics in Johannesburg. Predictors of MTCT (positive infant HIV DNA polymerase chain reaction at 4-6 weeks) were assessed with multivariate logistic regression. Results: Mean age was 30.2 years (SD = 5.0) and median baseline CD4 count was 161 cells per cubic millimeter (SD = 84.3). HAART duration at time of delivery was a mean 10.7 weeks (SD = 7.4) for the 86% of women who initiated treatment during pregnancy and 93.4 weeks (SD = 37.7) for those who became pregnant on HAART. Overall MTCT rate was 4.9% (43 of 874), with no differences detected between HAART regimens. MTCT rates were lower in women who became pregnant on HAART than those initiating HAART during pregnancy (0.7% versus 5.7%; P = 0.01). In the latter group, each additional week of treatment reduced odds of transmission by 8% (95% confidence interval: 0.87 to 0.99, P = 0.02). Conclusions: Late initiation of HAART is associated with increased risk of MTCT. Strategies are needed to facilitate earlier identification of HIV-infected women.

**Address:** Hoffman, Rm, Univ Calif Los Angeles, Div Infect Dis, David Geffen Sch Med, 10833 Le Conte Ave 37-121 Chs, Los Angeles, CA 90095 USA. rhoffman@mednet.ucla.edu


**Abstr.** SETTING: In July 2005, Medecins Sans Frontieres and the Ministry of Health, Kenya, implemented an integrated tuberculosis-human immunodeficiency virus (TB-HIV) programme in western Kenya. OBJECTIVE: To evaluate the impact of an integrated TB-HIV programme on patient care and TB programme outcomes. DESIGN: Retrospective evaluation of three time periods: before (January-June 2005), shortly after (January-June 2006) and medium term after (January-December 2007) the implementation of the integrated programme. RESULTS: Respectively 79% and 91% of TB patients were HIV tested shortly and at medium term after service integration. The HIV-positive rate varied from 96% before the intervention to respectively 88% (305/347) and 74% (301/405) after. The estimated number of HIV-positive cases was respectively 303, 323 and 331 in the three periods. The proportion of patients receiving cotrimoxazole prophylaxis increased significantly from 47% (142/303) to 94% (303/323) and 86% (285/331, P < 0.05). Before the intervention, 87% (171/197) of the TB-HIV patients would have been missed when initiating antiretroviral treatment, compared to respectively 29% (60/210) and 36% (78/215) after the integration. The TB programme success rate increased from 56% (230/409) to 71% (319/447) in the third period (P < 0.05); however, there was no significant decrease in the default rate: 20% to 22% (P = 0.66) and 18% (P = 0.37). CONCLUSION: Integrated TB-HIV care has a very positive impact on the management of TB-HIV patients and on TB treatment outcomes.

**Address:** Huerga, H, Med Sans Frontieres, French Off, Abc Pl,Waiyaki Way,Pob 39719, Nairobi, Kenya. helena.huerga@paris.msf.org


**Notes.** Patel paper editorial

**Address:** Kourtis, Ap, Ctr Dis Control & Prevent, Div Reprod Hlth, Nccdphp, 4770 Buford Hwy Ne,Msk34, Atlanta, GA 30341 USA. apk3@cdc.gov

**Free Full Text:** [http://www.journals.uchicago.edu/doi/pdf/10.1086/651233](http://www.journals.uchicago.edu/doi/pdf/10.1086/651233)

Abstr. Background. Cryptococcal meningitis (CM) remains a leading cause of acquired immunodeficiency syndrome-related death in sub-Saharan Africa. The timing of the initiation of antiretroviral therapy (ART) for human immunodeficiency virus (HIV)-associated CM remains uncertain. The study aimed to determine the optimal timing for initiation of ART in HIV-positive individuals with CM. Methods. A prospective, open-label, randomized clinical trial was conducted at a tertiary teaching hospital in Zimbabwe. Participants were aged >= 18 years, were ART naive, had received a first CM diagnosis, and were randomized to receive early ART (within 72 h after CM diagnosis) or delayed ART (after 10 weeks of treatment with fluconazole alone). Participants received 800 mg of fluconazole per day. The ART regimen used was stavudine, lamivudine, and nevirapine given twice daily. The duration of follow-up was up to 3 years. The primary end point was all-cause mortality. Results. Fifty-four participants were enrolled in the study (28 in the early ART arm and 26 in the delayed ART arm). The median CD4 cell count at enrollment was 37 cells/mm(3) (interquartile range, 17-69 cells/mm(3)). The 3-year mortality rate differed significantly between the early and delayed ART groups (88% vs 54%; P<.006); the overall 3-year mortality rate was 73%. The median durations of survival were 28 days and 637 days in the early and delayed ART groups, respectively (Pp. 031, by log-rank test). The risk of mortality was almost 3 times as great in the early ART group versus the delayed ART group (adjusted hazard ratio, 2.85; 95% confidence interval, 1.1-7.23). The study was terminated early by the data safety monitoring committee. Conclusions. In resource-limited settings where CM management may be suboptimal, when compared with a delay of 10 weeks after a CM diagnosis, early initiation of ART results in increased mortality.

Address: Makadzange, At, Univ Washington, Dept Med, 1959 Ne Pacific St,Box 356421, Seattle, WA 98195 USA. tarirom@u.washington.edu

Free Full Text: http://www.journals.uchicago.edu/doi/pdf/10.1086/652652


Notes. Makadzange paper editorial

Address: Wilkinson, Rj, Univ Cape Town, Inst Infect Dis & Mol Med, Fac Hlth Sci, Rm 3-03-05, Za-7925 Observatory, South Africa. r.j.wilkinson@imperial.ac.uk

Free Full Text: http://www.journals.uchicago.edu/doi/pdf/10.1086/652653


Abstr. Objectives: To describe reasons for exclusion from isoniazid tuberculosis preventive therapy (IPT) and outcomes of persons living with HIV (PLWH) during 6 months of IPT. Methods: In a clinical trial conducted in government clinics, first screening (screen 1) used National IPT Program guidelines and a second screening (screen 2) was trial specific. Adherence was defined as attending 6 monthly visits. Results: Between 2004 and 2006, at 4018 screening visits, 2934 (73%) PLWH met screen 1 criteria; 1995 (68%) met screen 2 criteria and were enrolled. Major reasons for exclusion were illness (66%) at screen 1 and abnormal chest radiographs (36%) at screen 2. Tuberculin skin tests were >= 5 mm in 24% of those enrolled and 31% had CD4 lymphocyte counts <200 cells/mm(3). During the 6 months, 8 (0.40%) developed tuberculosis disease, 28 (1.4%) had severe adverse events (19/28 were hepatitis including one death probably isoniazid-associated), 20 others died, and 22% initiated antiretroviral therapy (ART). Although adherence was 86%, being on ART improved adherence: relative risk 1.41 (95% confidence limits 1.04-1.91). In multivariate analysis, ART was associated with a 4.38 greater odds of adherence to IPT. Conclusions: Six months of IPT was relatively safe and well-tolerated by PLWH. Adherence to IPT was significantly better among those receiving ART with IPT.

Abstract edited. Background. Conflicting results have been reported among studies of protease inhibitor (PI) use during pregnancy and preterm birth. Uncontrolled confounding by indication may explain some of the differences among studies. Methods. In total, 777 human immunodeficiency virus (HIV)-infected pregnant women in a prospective cohort who were not receiving antiretroviral (ARV) treatment at conception were studied. Births <37 weeks gestation were reviewed, and deliveries due to spontaneous labor and/or rupture of membranes were identified. Risk of preterm birth and low birth weight (<2500 g) were evaluated by using multivariable logistic regression. Results. Of the study population, 558 (72%) received combination ARV with PI during pregnancy, and a total of 130 preterm births were observed. Main combination ARV included zidovudine and lamivudine, plus nelfinavir or lopinavir/ritonavir in the PI group and abacavir or nevirapine in the non PI group. In adjusted analyses, combination ARV with PI was not significantly associated with spontaneous preterm birth, compared to ARV without PI (odds ratio [OR], 1.22; 95% confidence interval [CI], 0.70-2.12). Sensitivity analyses that included women who received ARV prior to pregnancy also did not identify a significant association (OR, 1.34; 95% CI, 0.84-2.16). Low birth weight results were similar. No evidence of an association between use of combination ARV with PI during pregnancy and preterm birth was found. Our study supports current guidelines that promote consideration of combination ARV for all HIV-infected pregnant women.


Abstr. Objective: To determine the efficacy of patient-selected treatment partners on virologic and adherence outcomes during first-line antiretroviral therapy. Design: Randomized controlled trial. Setting and Analytical Approach: Between June 2006 and December 2007, 499 HIV-infected adults in Jos, Nigeria, were randomized to standard of care (SOC) or patient-selected treatment partner-assisted therapy (TPA). Each patient was followed for 48 weeks. Virologic outcomes, adherence to drug pick-up, CD4 cell counts, and mortality are reported. Results: At week 24, undetectable viral load was achieved by 61.7% of patients in the TPA arm versus 50.2% of those receiving SOC [odds ratio (OR) = 1.58, 95% CI: 1.11 to 2.26, P < 0.05]. There was no significant difference at week 48: 65.3% versus 59.4% for TPA and SOC, respectively (OR = 1.28, 95% CI: 0.89 to 1.84, P > 0.05). The TPA group had more than 3 times the odds of at least 95% drug pickup adherence through week 24 (OR = 3.06, 95% CI: 1.89 to 4.94, P < 0.01) and almost twice the odds through week 48 (OR = 1.95, 95% CI: 1.29 to 2.93, P < 0.01). At week 48, there were no significant differences in CD4 cell count increases (t = -0.09, df = 404, P > 0.05) or mortality (10.6% vs. 6.1%) between TPA vs. SOC, respectively. Residence-to-clinic distance was significantly associated with virologic and adherence outcomes. Conclusions: Use of patient-selected treatment partners was associated with improved drug pickup adherence and initial virologic success but had no durable effect on attaining undetectable viral load.

Taiwo, Bo, Northwestern Univ, Div Infect Dis, Feinberg Sch Med, 645 N Michigan Ave, Suite 900, Chicago, IL 60611 USA. b-taiwo@northwestern.edu