



World Health
Organization

anRS

French National Agency
for Research on AIDS
and Viral Hepatitis



ELIZABETH GLASER
PEDIATRIC AIDS FOUNDATION

JOINTHEMOMENT
create a generation free of HIV

Monthly
Intelligence
Report

2011

Vol.7 - Issue 2

[Back Issues on Line](#)

HIV Care & PMTCT in Resource-Limited Settings

prepared by the Bordeaux Working Group

Members:

- Elise Arrivé
- Renaud Becquet
- Mathias Bruyand
- François Dabis (Chair)
- Antoine Jaquet
- Valériane Leroy
- Charlotte Lewden
- Evelyne Mouillet (Coordinator)
- Camille Ndongki
- Joanna Orne-Gliemann (Coordinator)
- Hapsatou Touré



Number of citations selected for this issue: **19**

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

Alcorn K. **European Medicines Agency: d4T to be used only in last resort [News]**. Aidsmap 2011.

Free Full Text: <http://www.aidsmap.com/page/1672701>

Aluisio A, Richardson BA, Bosire R, John-Stewart G, Mbori-Ngacha D, Farquhar C. **Male antenatal attendance and HIV testing are associated with decreased infant HIV infection and increased HIV-free survival.** *J Acquir Immune Defic Syndr* 2011;56(1):76-82.

Abstr. OBJECTIVE: To investigate the relationship between male involvement in prevention of mother-to-child HIV transmission services and infant HIV acquisition and mortality, a prospective cohort study was undertaken between 1999 and 2005 in Nairobi, Kenya. METHODS: HIV-infected pregnant women were enrolled and followed with their infants for 1 year with infant HIV DNA testing at birth, 1, 3, 6, 9, and 12 months postpartum. Women were encouraged to invite male partners for prevention counseling and HIV testing. RESULTS: Among 456 female participants, 140 partners (31%) attended the antenatal clinic. Eighty-two (19%) of 441 infants tested were HIV infected by 1 year of age. Adjusting for maternal viral load, vertical transmission risk was lower among women with partner attendance compared with those without [adjusted hazard ratio (aHR) = 0.56, 95% confidence interval (CI): 0.33 to 0.98; P = 0.042] and among women reporting versus not reporting previous partner HIV testing (aHR = 0.52, 95% CI: 0.32 to 0.84; P = 0.008). The combined risk of HIV acquisition or infant mortality was lower with male attendance (aHR = 0.55; 95% CI: 0.35 to 0.88; P = 0.012) and report of prior male HIV testing (aHR = 0.58; 95% CI: 0.34 to 0.88; P = 0.01) when adjusting for maternal viral load and breastfeeding. CONCLUSIONS: Including men in antenatal prevention of mother-to-child HIV transmission services with HIV testing may improve infant health outcomes.

Address: Stony Brook University Medical Center, Stony Brook, NY, USA.
adam.aluisio@hsc.stonybrook.edu

Bendavid E, Grant P, Talbot A, Owens DK, Zolopa A. **Cost-effectiveness of antiretroviral regimens in the World Health Organization's treatment guidelines: a South African analysis.** *AIDS* 2011;25(2):211-20.

Abstr. OBJECTIVE: the World Health Organization (WHO) recently changed its first-line antiretroviral treatment guidelines in resource-limited settings. The cost-effectiveness of the new guidelines is unknown. DESIGN: comparative effectiveness and cost-effectiveness analysis using a model of HIV disease progression and treatment. METHODS: using a simulation of HIV disease and treatment in South Africa, we compared the life expectancy, quality-adjusted life expectancy, lifetime costs, and cost-effectiveness of five initial regimens. Four are currently recommended by the WHO: tenofovir / lamivudine / efavirenz; tenofovir / lamivudine / nevirapine; zidovudine/lamivudine/efavirenz; and zidovudine/lamivudine/nevirapine. The fifth is the most common regimen in current use: stavudine/lamivudine/nevirapine. Virologic suppression and toxicities determine regimen effectiveness and cost-effectiveness. RESULTS: choice of first-line regimen is associated with a difference of nearly 12 months of quality-adjusted life expectancy, from 135.2 months (tenofovir/lamivudine/efavirenz) to 123.7 months (stavudine/lamivudine/nevirapine). Stavudine/lamivudine/nevirapine is more costly and less effective than zidovudine/lamivudine/nevirapine. Initiating treatment with a regimen containing tenofovir/lamivudine/nevirapine is associated with an incremental cost-effectiveness ratio of \$1045 per quality-adjusted life year compared with zidovudine/lamivudine/nevirapine. Using tenofovir/lamivudine/efavirenz was associated with the highest survival, fewest opportunistic diseases, lowest rate of regimen substitution, and an incremental cost-effectiveness ratio of \$5949 per quality-

adjusted life year gained compared with tenofovir/lamivudine/nevirapine. Zidovudine/lamivudine/efavirenz was more costly and less effective than tenofovir/lamivudine/nevirapine. Results were sensitive to the rates of toxicities and the disutility associated with each toxicity. **CONCLUSION:** among the options recommended by WHO, we estimate only three should be considered under normal circumstances. Choice among those depends on available resources and willingness to pay. Stavudine/lamivudine/nevirapine is associated with the poorest quality-adjusted survival and higher costs than zidovudine/lamivudine/nevirapine.

Address: Division of General Internal Medicine, Stanford University, Stanford, USA. ebd@stanford.edu

Braun M, Kabue MM, McCollum ED, Ahmed S, Kim M, Aertker L, Chirwa M, Eliya M, Mofolo I, Hoffman I, Kazembe PN, van der Horst C, Kline MW, Hosseinipour MC. **Inadequate Coordination of Maternal and Infant HIV Services Detrimentially Affects Early Infant Diagnosis Outcomes in Lilongwe, Malawi.** *J Acquir Immune Defic Syndr* 2011 Epub.

Abstr. **OBJECTIVE:** To assess the continuity of care and outcome of pediatric HIV prevention, testing, and treatment services, focusing on early infant diagnosis with DNA polymerase chain reaction (PCR). **DESIGN::** A retrospective observational cohort. **METHODS::** Maternal HIV antibody, infant HIV DNA PCR test results, and outcome data from HIV-infected infants from the prevention of mother-to-child transmission, early infant diagnosis, and pediatric HIV treatment programs operating in Lilongwe, Malawi, between 2004 and 2008 were collected, merged, and analyzed. **RESULTS::** Of the 14,669 pregnant women who tested HIV antibody positive, 7875 infants (53.7%) received HIV DNA PCR testing. One thousand eighty-four infants (13.8%) were HIV infected. Three hundred twenty (29.5%) children enrolled into pediatric HIV care, with 202 (63.1%) at the Baylor Center of Excellence. Among these, antiretroviral therapy was initiated on 110 infants (54.5%) whose median age was 9.1 months (interquartile range, 5.4-13.8) and a median of 2.5 months (interquartile range, 1.4-5.2) after HIV clinic registration. Sixty-nine HIV-infected infants (34.2%) died or were lost by December 2008. Initiation of antiretroviral therapy increased the likelihood of survival 7-fold (odds ratio, 7.1; 95% confidence interval, 3.68 to 13.70). **CONCLUSIONS::** Separate programs for maternal and infant HIV prevention and care services demonstrated high attrition rates of HIV-exposed and HIV-infected infants, elevated levels of mother-to-child transmission, late infant diagnosis, delayed pediatric antiretroviral therapy initiation, and high HIV-infected infant mortality. Antiretroviral therapy increased HIV-infected infant survival, emphasizing the urgent need for improved service coordination and strategies that increase access to infant HIV diagnosis, improve patient retention, and reduce antiretroviral therapy initiation delays.

Brust JC, Lygizos M, Chaiyachati K, Scott M, van der Merwe TL, Moll AP, Li X, Loveday M, Bamber SA, Lalloo UG, Friedland GH, Shah NS, Gandhi NR. **Culture Conversion Among HIV Co-Infected Multidrug-Resistant Tuberculosis Patients in Tugela Ferry, South Africa.** *PLoS One* 2011;6(1):e15841.

Abstr. **BACKGROUND:** Little is known about the time to sputum culture conversion in MDR-TB patients co-infected with HIV, although such patients have, historically, had poor outcomes. We describe culture conversion rates among MDR-TB patients with and without HIV-co-infection in a TB-endemic, high-HIV prevalent, resource-limited setting. **METHODS:** Patients with culture-proven MDR-TB were treated with a standardized second-line regimen. Sputum cultures were taken monthly and conversion was defined as two negative cultures taken at least one month apart. Time-to-conversion was measured from the day of initiation of MDR-TB therapy. Subjects with HIV received antiretroviral therapy (ART) regardless of CD4 count. **RESULTS:** Among 45 MDR-TB

patients, 36 (80%) were HIV-co-infected. Overall, 40 (89%) of the 45 patients culture-converted within the first six months and there was no difference in the proportion who converted based on HIV status. Median time-to-conversion was 62 days (IQR 48-111). Among the five patients who did not culture convert, three died, one was transferred to another facility, and one refused further treatment before completing 6 months of therapy. Thus, no patients remained persistently culture-positive at 6 months of therapy. CONCLUSIONS: With concurrent second-line TB and ART medications, MDR-TB/HIV co-infected patients can achieve culture conversion rates and times similar to those reported from HIV-negative patients worldwide. Future studies are needed to examine whether similar cure rates are achieved at the end of MDR-TB treatment and to determine the optimal use and timing of ART in the setting of MDR-TB treatment.

Address: Department of Medicine, Montefiore Medical Center and Albert Einstein College of Medicine, Bronx, New York, United States of America. jcmbrust@gmail.com

Free Full Text: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3022524/pdf/pmed.1000391.pdf>

Cook RE, Ciampa PJ, Sidat M, Blevins M, Burlison J, Davidson MA, Arroz JA, Vergara AE, Vermund SH, Moon TD. **Predictors of successful early infant diagnosis of HIV in a rural district hospital in Zambezia, Mozambique.** J Acquir Immune Defic Syndr 2011 Epub.

Abstr. BACKGROUND: A key challenge inhibiting the timely initiation of pediatric antiretroviral treatment is the loss to follow-up of mothers and their infants between the time of mothers' HIV diagnoses in pregnancy and return after delivery for early infant diagnosis (EID) of HIV. We sought to identify barriers to follow-up of HIV-exposed infants in rural Zambezia Province, Mozambique. METHODS: We determined follow-up rates for early infant diagnosis and age at first test in a retrospective cohort of 443 HIV-infected mothers and their infants. Multivariable logistic regression models were used to identify factors associated with successful follow-up. RESULTS: Of the 443 mother-infant pairs, 217 (49%) mothers enrolled in the adult HIV care clinic, and only 110 (25%) infants were brought for early infant diagnosis. The predictors of follow-up for EID were larger household size (OR=1.30; 95% CI, 1.09-1.53), independent maternal source of income (OR=10.8; 95% CI, 3.42-34.0), greater distance from the hospital (OR=2.14; 95% CI, 1.01-4.51) and maternal receipt of ART (OR=3.15; 95% CI, 1.02-9.73). The median age at first test among 105 infants was 5 months (interquartile range 2 to 7); 16% of the tested infants were infected. CONCLUSIONS: Three of four HIV-infected women in rural Mozambique did not bring their children for early infant HIV diagnosis. Maternal receipt of ART has favorable implications for maternal health that will increase the likelihood of early infant diagnosis. We are working with local health authorities to improve the linkage of HIV-infected women to HIV care to maximize early infant diagnosis and care.

Dryden-Peterson S, Shapiro RL, Hughes MD, Powis K, Ogwu A, Moffat C, Moyo S, Makhema J, Essex M, Lockman S. **Increased Risk of Severe Infant Anemia Following Exposure to Maternal HAART, Botswana.** J Acquir Immune Defic Syndr 2011.

Abstr. BACKGROUND: Maternal highly-active antiretroviral therapy (HAART) reduces mother-to-child HIV transmission (MTCT), but may increase the risk for infant anemia. METHODS: The incidence of first severe anemia (Grade 3 or 4, Division of AIDS 2004 Toxicity Table) was assessed among HIV-uninfected infants in the Mashai and Mma Bana MTCT prevention trials in Botswana. Severe anemia rates were compared between 3 groups: infants exposed to maternal HAART in utero and during breastfeeding and 1 month of postnatal zidovudine (HAART-BF); infants exposed to maternal zidovudine (ZDV) in utero, 6 months of postnatal ZDV, and breastfeeding (ZDV-BF); and infants exposed to maternal ZDV in utero, 1 month of postnatal ZDV, and formula-feeding (ZDV-

FF). RESULTS: A total of 1719 infants were analyzed- 691 HAART-BF, 503 ZDV-BF, and 525 ZDV-FF. Severe anemia was detected in 118 infants (7.4%). By 6 months, 12.5% of HAART-BF infants experienced severe anemia, compared with 5.3% of ZDV-BF ($P < 0.001$) and 2.5% of ZDV-FF infants ($P < 0.001$). In adjusted analysis, HAART-BF infants were at greater risk of severe anemia than ZDV-BF or ZDV-FF infants (adjusted odds ratios 2.6 and 5.8, respectively; $P < 0.001$). Most anemias were asymptomatic and improved with iron/multivitamin supplementation and cessation of ZDV exposure. However, 11 infants (0.6% of all infants) required transfusion for symptomatic anemia. Microcytosis and hypochromia were common among infants with severe anemia. CONCLUSIONS: Exposure to maternal HAART starting in utero was associated with severe infant anemia. Confirmation of this finding and possible strategies to mitigate hematologic toxicity warrant further study.

Egger M, Spycher BD, Sidle J, Weigel R, Geng EH, Fox MP, Macphail P, van Cutsem G, Messou E, Wood R, Nash D, Pascoe M, Dickinson D, Etard JF, McIntyre JA, Brinkhof MW. **Correcting mortality for loss to follow-up: a nomogram applied to antiretroviral treatment programmes in sub-saharan Africa.** PLoS Med 2011;8(1):e1000390.

Abstr. BACKGROUND: The World Health Organization estimates that in sub-Saharan Africa about 4 million HIV-infected patients had started antiretroviral therapy (ART) by the end of 2008. Loss of patients to follow-up and care is an important problem for treatment programmes in this region. As mortality is high in these patients compared to patients remaining in care, ART programmes with high rates of loss to follow-up may substantially underestimate mortality of all patients starting ART. METHODS AND FINDINGS: We developed a nomogram to correct mortality estimates for loss to follow-up, based on the fact that mortality of all patients starting ART in a treatment programme is a weighted average of mortality among patients lost to follow-up and patients remaining in care. The nomogram gives a correction factor based on the percentage of patients lost to follow-up at a given point in time, and the estimated ratio of mortality between patients lost and not lost to follow-up. The mortality observed among patients retained in care is then multiplied by the correction factor to obtain an estimate of programme-level mortality that takes all deaths into account. A web calculator directly calculates the corrected, programme-level mortality with 95% confidence intervals (CIs). We applied the method to 11 ART programmes in sub-Saharan Africa. Patients retained in care had a mortality at 1 year of 1.4% to 12.0%; loss to follow-up ranged from 2.8% to 28.7%; and the correction factor from 1.2 to 8.0. The absolute difference between uncorrected and corrected mortality at 1 year ranged from 1.6% to 9.8%, and was above 5% in four programmes. The largest difference in mortality was in a programme with 28.7% of patients lost to follow-up at 1 year. CONCLUSIONS: The amount of bias in mortality estimates can be large in ART programmes with substantial loss to follow-up. Programmes should routinely report mortality among patients retained in care and the proportion of patients lost. A simple nomogram can then be used to estimate mortality among all patients who started ART, for a range of plausible mortality rates among patients lost to follow-up. Please see later in the article for the Editors' Summary.

Address: Institute of Social and Preventive Medicine (ISPM), University of Bern, Switzerland. egger@ispm.unibe.ch

Free Full Text: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3022522/pdf/pmed.1000390.pdf>

Getahun H, Kittikraisak W, Heilig CM, Corbett EL, Ayles H, Cain KP, Grant AD, Churchyard GJ, Kimerling M, Shah S, Lawn SD, Wood R, Maartens G, Granich R, Date AA, Varma JK. **Development of a Standardized Screening Rule for Tuberculosis in People Living with HIV in Resource-Constrained Settings: Individual Participant Data Meta-analysis of Observational Studies.** PLoS Med 2011;8(1):e1000391.

Abstr. BACKGROUND: The World Health Organization recommends the screening of all people living with HIV for tuberculosis (TB) disease, followed by TB treatment, or isoniazid preventive therapy (IPT) when TB is excluded. However, the difficulty of reliably excluding TB disease has severely limited TB screening and IPT uptake in resource-limited settings. We conducted an individual participant data meta-analysis of primary studies, aiming to identify a sensitive TB screening rule. METHODS AND FINDINGS: We identified 12 studies that had systematically collected sputum specimens regardless of signs or symptoms, at least one mycobacterial culture, clinical symptoms, and HIV and TB disease status. Bivariate random-effects meta-analysis and the hierarchical summary relative operating characteristic curves were used to evaluate the screening performance of all combinations of variables of interest. TB disease was diagnosed in 557 (5.8%) of 9,626 people living with HIV. The primary analysis included 8,148 people living with HIV who could be evaluated on five symptoms from nine of the 12 studies. The median age was 34 years. The best performing rule was the presence of any one of: current cough (any duration), fever, night sweats, or weight loss. The overall sensitivity of this rule was 78.9% (95% confidence interval [CI] 58.3%-90.9%) and specificity was 49.6% (95% CI 29.2%-70.1%). Its sensitivity increased to 90.1% (95% CI 76.3%-96.2%) among participants selected from clinical settings and to 88.0% (95% CI 76.1%-94.4%) among those who were not previously screened for TB. Negative predictive value was 97.7% (95% CI 97.4%-98.0%) and 90.0% (95% CI 88.6%-91.3%) at 5% and 20% prevalence of TB among people living with HIV, respectively. Abnormal chest radiographic findings increased the sensitivity of the rule by 11.7% (90.6% versus 78.9%) with a reduction of specificity by 10.7% (49.6% versus 38.9%). CONCLUSIONS: Absence of all of current cough, fever, night sweats, and weight loss can identify a subset of people living with HIV who have a very low probability of having TB disease. A simplified screening rule using any one of these symptoms can be used in resource-constrained settings to identify people living with HIV in need of further diagnostic assessment for TB. Use of this algorithm should result in earlier TB diagnosis and treatment, and should allow for substantial scale-up of IPT. Please see later in the article for the Editors' Summary.

Address: World Health Organization, Geneva, Switzerland. getahunh@who.int

Free Full Text: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3022524/pdf/pmed.1000391.pdf>

Imani PD, Musoke P, Byarugaba J, Tumwine JK. **Human immunodeficiency virus infection and cerebral malaria in children in Uganda: a case-control study.** BMC Pediatr 2011;11(1):5.

Abstr. ABSTRACT: BACKGROUND: Human immunodeficiency virus (HIV)-1 infection increases the burden of malaria by increasing susceptibility to infection and decreasing the response to malarial treatment. HIV-1 has also been found to suppress the immune system and predispose to severe forms of malaria in adults. There is still a paucity of data on the association between HIV-1 infection and cerebral malaria in children. The aim of this study was to determine whether HIV-1 infection is a risk factor for cerebral malaria in children. METHOD: We conducted an unmatched case-control study, in which 100 children with cerebral malaria were compared with 132 with uncomplicated malaria and 120 with no malaria. In stratified analyses we estimated odds ratios (ORs) and 95% confidence intervals (CIs) adjusted for age. RESULTS: HIV-1 infection was present in 9% of children with cerebral malaria compared to 2.3% in uncomplicated malaria (age-adjusted odds ratio (aOR) 5.94 (95% confidence interval (CI) 1.36-25.94, p=0.012); and 2.5% in children with no malaria (aOR 3.85 (95% CI 0.99-14.93, p= 0.037). The age-

adjusted odds of being HIV-positive among children with cerebral malaria compared to the control groups (children with uncomplicated malaria and no malaria) was 4.98 (95% CI 1.54-16.07), p-value=0.003. CONCLUSIONS: HIV-1 infection is associated with clinical presentation of cerebral malaria in children. Clinicians should ensure that children diagnosed with HIV infection are initiated on cotrimoxazole prophylaxis as soon as the diagnosis is made and caretakers counselled on the importance of adherence to the cotrimoxazole towards reducing the risk of acquiring *P.falciparum* malaria and associated complications such as cerebral malaria. Other malaria preventive measures such as use of insecticide-treated mosquito nets should also be emphasized during counselling sessions.

Free Full Text: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3035590/pdf/1471-2431-11-5.pdf>

Kapito-Tembo A, Meshnick SR, van Hensbroek MB, Phiri K, Fitzgerald M, Mwapasa V. **Marked Reduction in Prevalence of Malaria Parasitemia and Anemia in HIV-Infected Pregnant Women Taking Cotrimoxazole With Or Without Sulfadoxine-Pyrimethamine Intermittent Preventive Therapy during Pregnancy in Malawi.** *J Infect Dis* 2011;203(4):464-72.

Abstr. Background. Effectiveness of cotrimoxazole (CTX) compared with sulfadoxine-pyrimethamine (SP) intermittent-preventive-therapy (IPTp) for malaria in HIV-infected pregnant women is unknown. We examined effectiveness of CTX with or without SP-IPTp versus SP-IPTp at reducing malaria parasitemia and anemia. Methods. From 2005 to 2009, we conducted a cross-sectional study of HIV-infected pregnant women at Thyolo Hospital, Malawi. Blood was tested for malaria parasitemia and anemia (hemoglobin < 11g/dl). Data were collected on use of anti-malaria interventions and other risk factors. CTX prophylaxis policy for HIV-infected pregnant women was introduced in 2007, but implementation problems resulted in some women receiving both CTX and SP-IPTp. Findings. We enrolled 1,142 women, of whom 1,121 had data on CTX and/or SP-IPTp intake. Of these, 49.7%, 29.8%, and 15.4% reported taking SP-IPTp only, CTX only and SP-IPTp plus CTX, respectively. Compared with women taking SP-IPTp, those taking SP-IPTp plus CTX and CTX were less likely to have malaria parasitemia (OR, [95%CI]: 0.09, [0.01-0.66] and 0.43, [0.19-0.97], respectively) or anemia (PR, [95% CI]: 0.67, [0.54-0.83] and 0.72, [0.61-0.83], respectively). Conclusion. In HIV-infected pregnant women, daily CTX was associated with reduced malaria parasitemia and anemia compared with SP-IPTp. CTX plus SP-IPTp was associated with further reduction in malaria parasitemia but toxicity was not fully assessed.

Free Full Text: <http://jid.oxfordjournals.org/content/203/4/464.full.pdf+html>

Kesho Bora Study Group. **Triple antiretroviral compared with zidovudine and single-dose nevirapine prophylaxis during pregnancy and breastfeeding for prevention of mother-to-child transmission of HIV-1 (Kesho Bora study): a randomised controlled trial.** *Lancet Infect Dis* 2011 Epub.

Abstr. BACKGROUND: Breastfeeding is essential for child health and development in low-resource settings but carries a significant risk of transmission of HIV-1, especially in late stages of maternal disease. We aimed to assess the efficacy and safety of triple antiretroviral compared with zidovudine and single-dose nevirapine prophylaxis in pregnant women infected with HIV. METHODS: Pregnant women with WHO stage 1, 2, or 3 HIV-1 infection who had CD4 cell counts of 200-500 cells per μ L were enrolled at five study sites in Burkina Faso, Kenya, and South Africa to start study treatment at 28-36 weeks' gestation. Women were randomly assigned (1:1) by a computer generated random sequence to either triple antiretroviral prophylaxis (a combination of 300 mg zidovudine, 150 mg lamivudine, and 400 mg lopinavir plus 100 mg ritonavir twice daily

until cessation of breastfeeding to a maximum of 6.5 months post partum) or zidovudine and single-dose nevirapine (300 mg zidovudine twice daily until delivery and a dose of 600 mg zidovudine plus 200 mg nevirapine at the onset of labour and, after a protocol amendment in December, 2006, 1 week post-partum zidovudine 300 mg twice daily and lamivudine 150 mg twice daily). All infants received a 0.6 mL dose of nevirapine at birth and, from December, 2006, 4 mg/kg twice daily of zidovudine for 1 week after birth. Patients and investigators were not masked to treatment. The primary endpoints were HIV-free infant survival at 6 weeks and 12 months; HIV-free survival at 12 months in infants who were ever breastfed; AIDS-free survival in mothers at 18 months; and serious adverse events in mothers and babies. Analysis was by intention to treat. This trial is registered with Current Controlled Trials, ISRCTN71468401. FINDINGS: From June, 2005, to August, 2008, 882 women were enrolled, 824 of whom were randomised and gave birth to 805 singleton or first, liveborn infants. The cumulative rate of HIV transmission at 6 weeks was 3.3% (95% CI 1.9-5.6%) in the triple antiretroviral group compared with 5.0% (3.3-7.7%) in the zidovudine and single-dose nevirapine group, and at 12 months was 5.4% (3.6-8.1%) in the triple antiretroviral group compared with 9.5% (7.0-12.9%) in the zidovudine and single-dose nevirapine group ($p=0.029$). The cumulative rate of HIV transmission or death at 12 months was 10.2% (95% CI 7.6-13.6%) in the triple antiretroviral group compared with 16.0% (12.7-20.0%) in the zidovudine and single-dose nevirapine group ($p=0.017$). In infants whose mothers declared they intended to breastfeed, the cumulative rate of HIV transmission at 12 months was 5.6% (95% CI 3.4-8.9%) in the triple antiretroviral group compared with 10.7% (7.6-14.8%) in the zidovudine and single-dose nevirapine group ($p=0.02$). AIDS-free survival in mothers at 18 months will be reported in a different publication. The incidence of laboratory and clinical serious adverse events in both mothers and their babies was similar between groups. INTERPRETATION: Triple antiretroviral prophylaxis during pregnancy and breastfeeding is safe and reduces the risk of HIV transmission to infants. Revised WHO guidelines now recommend antiretroviral prophylaxis (either to the mother or to the baby) during breastfeeding if the mother is not already receiving antiretroviral treatment for her own health. FUNDING: Agence nationale de recherches sur le sida et les hepatites virales, Department for International Development, European and Developing Countries Clinical Trials Partnership, Thrasher Research Fund, Belgian Directorate General for International Cooperation, Centers for Disease Control and Prevention, Eunice Kennedy Shriver National Institute of Child Health and Human Development, and UNDP/UNFPA/World Bank/WHO Special Programme of Research, Development and Research Training in Human Reproduction.

Marston M, Becquet R, Zaba B, Moulton LH, Gray G, Coovadia H, Essex M, Ekouevi DK, Jackson D, Coutsooudis A, Kilewo C, Leroy V, Wiktor S, Nduati R, Msellati P, Dabis F, Newell ML, Ghys PD. **Net survival of perinatally and postnatally HIV-infected children: a pooled analysis of individual data from sub-Saharan Africa.** *Int J Epidemiol* 2011 Epub.

Abstr. BACKGROUND: Previously, HIV epidemic models have used a double Weibull curve to represent high initial and late mortality of HIV-infected children, without distinguishing timing of infection (peri- or post-natally). With more data on timing of infection, which may be associated with disease progression, a separate representation of children infected early and late was proposed. METHODS: Paediatric survival post-HIV infection without anti-retroviral treatment was calculated using pooled data from 12 studies with known timing of HIV infection. Children were grouped into perinatally or post-natally infected. Net mortality was calculated using cause-deleted life tables to give survival as if HIV was the only competing cause of death. To extend the curve beyond the available data, children surviving beyond 2.5 years post infection were assumed to have the same survival as young adults. Double Weibull curves were fitted to both extended survival curves to represent survival of children infected perinatally or through breastfeeding. RESULTS: Those children infected perinatally had a much higher risk of

dying than those infected through breastfeeding, even allowing for background mortality. The final-fitted double Weibull curves gave 75% survival at 5 months after infection for perinatally infected, and 1.1 years for post-natally infected children. An estimated 25% of the early infected children would still be alive at 10.6 years compared with 16.9 years for those infected through breastfeeding. CONCLUSIONS: The increase in available data has enabled separation of child mortality patterns by timing of infection allowing improvement and more flexibility in modelling of paediatric HIV infection and survival.

McGrath CJ, Chung MH, Richardson BA, Benki-Nugent S, Warui D, John-Stewart GC. **Younger age at HAART initiation is associated with more rapid growth reconstitution.** AIDS 2011;25(3):345-55.

Abstr. OBJECTIVES: Patterns of growth following highly active antiretroviral therapy (HAART) administration among children are not well defined. The objective of this study was to determine rates and predictors of growth reconstitution among children on HAART. METHODS: A study was conducted among HIV-1-infected children initiating HAART at an HIV treatment clinic in Kenya. Kaplan-Meier survival curves and Cox proportional hazards regression models compared catch-up growth (Z-score ≥ 0) at 12 months post-HAART. Multivariate linear mixed-effects models determined rates and predictors of growth following HAART. RESULTS: One hundred and seventy-three HIV-1-infected children initiated HAART with a median age of 4.7 years [interquartile range (IQR) 2.4, 7.0]. At baseline, children below 3 years had lower weight-for-age (WAZ) and weight-for-height (WHZ) Z-scores than children 3-5 and 6-10 years (WAZ: P = 0.03; WHZ: P = 0.006). Adjusting for baseline growth, children below 3 years were two to three-fold more likely to attain population age-norms (Z-score = 0) than 6-10 years (WAZ: P = 0.055; WHZ: P = 0.005) at 12 months post-HAART. After adjustment, children below 3 years had higher increases in WAZ and WHZ following HAART than 6-10 years (WAZ: P = 0.006; WHZ: P = 0.005). Children at WHO stage at least 3 at baseline experienced more rapid WHZ reconstitution (P = 0.002). Food supplementation while on HAART was associated with increased monthly gains in weight indices (WAZ: P = 0.001; WHZ: P = 0.005), and multivitamins were associated with greater increases in height (P < 0.01). CONCLUSION: Following HAART initiation, younger children had more rapid catch-up to the population-average weight of their peers than older children, demonstrating growth benefit of earlier HAART. In addition to HAART, food supplementation and multivitamins may also accelerate growth reconstitution.

Address: Department of Epidemiology, University of Washington, Seattle, Washington, USA. mcgrathc@u.washington.edu

Nglazi MD, Lawn SD, Kaplan R, Kranzer K, Orrell C, Wood R, Bekker LG. **Changes in programmatic outcomes during 7 years of scale-up at a community-based antiretroviral treatment service in South Africa.** J Acquir Immune Defic Syndr 2011;56(1):e1-8.

Abstr. OBJECTIVES: To assess sustainability of programmatic outcomes in a community-based antiretroviral therapy (ART) service in South Africa during 7 years of scale-up. METHODS: Prospective cohort of treatment-naive patients aged ≥ 15 years enrolled between 2002 and 2008. Data were analyzed by calendar period of ART initiation using time-to-event analysis and logistic regression. RESULTS: ART was initiated by 3162 patients (67% women; median age, 34 years) who were followed-up for a median of 2.4 years (interquartile range, 1.2-3.8). After 6 years, the cumulative probability of death and loss to follow-up (LTFU) was 37.4%. The probabilities of transfer-out to another ART service and of virological failure were 21.6% and 23.1%, respectively. Low mortality risk and excellent virological and immunological responses during the first year of ART were not associated with calendar period of ART initiation. In contrast, risk of LTFU and virological failure both increased between successive calendar periods in unadjusted and

adjusted analyses. The number of patients per member of clinic staff increased markedly over time. **CONCLUSIONS:** Successful early outcomes (low mortality and good immunological and virological responses) were sustained between sequential calendar periods during 7 years of scale-up. In contrast, the increasing cumulative probabilities of LTFU or virological failure may reflect decreasing capacity to adequately support patients during long-term therapy as clinic caseload escalated.

Address: The Desmond Tutu HIV Centre, Institute for Infectious Disease and Molecular Medicine, Department of Medicine, Faculty of Health Sciences, University of Cape Town, Cape Town, South Africa. mweete.nglazi@hiv-research.org.za

PENPACT-1 (PENTA 9/PACTG 390) Study Team. **First-line antiretroviral therapy with a protease inhibitor versus non-nucleoside reverse transcriptase inhibitor and switch at higher versus low viral load in HIV-infected children: an open-label, randomised phase 2/3 trial.** *Lancet Infect Dis* 2011.

Abstr. **BACKGROUND:** Children with HIV will be on antiretroviral therapy (ART) longer than adults, and therefore the durability of first-line ART and timing of switch to second-line are key questions. We assess the long-term outcome of protease inhibitor and non-nucleoside reverse transcriptase inhibitor (NNRTI) first-line ART and viral load switch criteria in children. **METHODS:** In a randomised open-label factorial trial, we compared effectiveness of two nucleoside reverse transcriptase inhibitors (NRTIs) plus a protease inhibitor versus two NRTIs plus an NNRTI and of switch to second-line ART at a viral load of 1000 copies per mL versus 30 000 copies per mL in previously untreated children infected with HIV from Europe and North and South America. Random assignment was by computer-generated sequentially numbered lists stratified by age, region, and by exposure to perinatal ART. Primary outcome was change in viral load between baseline and 4 years. Analysis was by intention to treat, which we defined as all patients that started treatment. This study is registered with ISRCTN, number ISRCTN73318385. **FINDINGS:** Between Sept 25, 2002, and Sept 7, 2005, 266 children (median age 6.5 years; IQR 2.8-12.9) were randomly assigned treatment regimens: 66 to receive protease inhibitor and switch to second-line at 1000 copies per mL (PI-low), 65 protease inhibitor and switch at 30 000 copies per mL (PI-higher), 68 NNRTI and switch at 1000 copies per mL (NNRTI-low), and 67 NNRTI and switch at 30 000 copies per mL (NNRTI-higher). Median follow-up was 5.0 years (IQR 4.2-6.0) and 188 (71%) children were on first-line ART at trial end. At 4 years, mean reductions in viral load were -3.16 log₁₀ copies per mL for protease inhibitors versus -3.31 log₁₀ copies per mL for NNRTIs (difference -0.15 log₁₀ copies per mL, 95% CI -0.41 to 0.11; p=0.26), and -3.26 log₁₀ copies per mL for switching at the low versus -3.20 log₁₀ copies per mL for switching at the higher threshold (difference 0.06 log₁₀ copies per mL, 95% CI -0.20 to 0.32; p=0.56). Protease inhibitor resistance was uncommon and there was no increase in NRTI resistance in the PI-higher compared with the PI-low group. NNRTI resistance was selected early, and about 10% more children accumulated NRTI mutations in the NNRTI-higher than the NNRTI-low group. Nine children had new CDC stage-C events and 60 had grade 3/4 adverse events; both were balanced across randomised groups. **INTERPRETATION:** Good long-term outcomes were achieved with all treatments strategies. Delayed switching of protease-inhibitor-based ART might be reasonable where future drug options are limited, because the risk of selecting for NRTI and protease-inhibitor resistance is low. **FUNDING:** Paediatric European Network for Treatment of AIDS (PENTA) and Pediatric AIDS Clinical Trials Group (PACTG/IMPACT).

Ruel TD, Kanya MR, Li P, Pasutti W, Charlebois ED, Liegler T, Dorsey G, Rosenthal PJ, Havlir DV, Wong JK, Achan J. **Early virologic failure and the development of antiretroviral drug resistance mutations in HIV-infected Ugandan children.** J Acquir Immune Defic Syndr 2011;56(1):44-50.

Abstr. BACKGROUND: Without virologic testing, HIV-infected African children starting antiretroviral (ARV) therapy are at risk for undetected virologic failure and the development of ARV resistance. We sought to determine the prevalence of early virologic failure (EVF), to characterize the evolution of ARV-resistance mutations and to predict the impact on second-line therapy. METHODS: The prevalence of EVF (HIV RNA >400 copies/mL on sequential visits after 6 months of therapy) was identified among 120 HIV-infected Ugandan children starting ARV therapy. ARV mutations were identified by population sequencing of HIV-1 pol in sequential archived specimens. Composite discrete genotypic susceptibility scores were determined for second-line ARV regimens. RESULTS: EVF occurred in 16 children (13%) and persisted throughout a median (interquartile ratio) 938 (760-1066) days of follow-up. M184V and nonnucleoside reverse transcriptase inhibitor-associated mutations emerged within 6 months of EVF; thymidine-analog-mutations arose after 12 months. Worse discrete genotypic susceptibility scores correlated with increasing duration of failure (Spearman R = -0.47; P = 0.001). Only 1 child met World Health Organization CD4 criteria for ARV failure at the time of EVF or during the follow-up period. CONCLUSIONS: A significant portion of HIV-infected African children experience EVF that would be undetected using CD4/clinical monitoring and resulted in the accumulation of ARV mutations that could compromise second-line therapy options.

Address: Department of Pediatrics, School of Medicine, University of California, San Francisco, San Francisco, CA 94143-0136, USA. ruelt@peds.ucsf.edu

Smart T. **Managing kidney disease in people with HIV in resource-limited settings.** HATIP 2011(173).

Free Full Text: <http://www.aidsmap.com/pdf/HATIP-173-February-11th-2011/page/1641212>

World Health Organisation. **HIV self-testing among health workers. A review of the literature and discussion of current practices, issues and options for increasing access to HIV testing in sub-Saharan Africa.** Geneva: World Health Organisation; 2011.

Free Full Text: http://whqlibdoc.who.int/publications/2011/9789241501033_eng.pdf



Institut de Santé Publique d'Épidémiologie et de Développement
Université Bordeaux Segalen
146 rue Leo-Saignat
33076 Bordeaux Cedex, FRANCE

Website:
<http://www.isped.u-bordeaux2.fr>

Contact:
Joanna ORNE-GLIEMANN
E-mail: Joanna.Orne-Gliemann@isped.u-bordeaux2.fr