Abstract Book

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ABSTRACTS

Oral presentations
Abstract: O_01

**HIV infection and adolescents**

**Determinants of HIV Serostatus Self-Disclosure Among Adolescents Participating in the Adolescent Impact Study**

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**Introduction:** Self-disclosure of positive HIV status can provide adolescents with support from family, friends, and sexual partners. It can also increase stigma, discrimination and rejection for the HIV-positive adolescent and his/her family. This study sought to examine the prevalence and predictors of self-disclosure in HIV-positive adolescents.

**Methods:** Data were collected at baseline assessment from participants enrolled in Adolescent Impact, an intervention study of risk behaviors and medication adherence among HIV-positive adolescents ages 13-21 (CDC-funded, IRB-approved). Self-disclosure, a dichotomized variable, defined as the revelation of information by an HIV-positive adolescent to a family member, peer or partner not previously aware of the adolescent’s serostatus, was determined through face-to-face and computer interviews; other data were obtained through medical records. Prevalence and predictors of self-disclosure of HIV status to others were determined using bivariate and multivariate logistic regression analysis.

**Results:** Of 166 participants (99 perinatally and 67 behaviorally infected; 47% male), 161 provided complete data. Self-disclosure of serostatus was reported by 94 youth (58%): 69% to family, 32% to friends, and 43% of those sexually experienced to partners. Bivariate analyses showed that older adolescents (18-21 years) were more likely to self-disclose than younger (13-17 years) (p<0.001), as were gay, lesbian, bisexual, and questioning adolescents versus heterosexual adolescents (p<0.04), those taking antiretroviral medications (p<0.002) and those living away from their families (p<0.02). Adolescents who had acquired HIV infection behaviorally were more than twice as likely to have disclosed their status as those with perinatal acquisition (87% vs. 36%, p<0.001). No differences were evident on the basis of gender, immunologic category, recent sexual activity, or reported number of close friends. In multivariate logistic regression analysis, the only behavioral acquisition of HIV independently predicted self-disclosure to others (AOR = 0.03, 95% Confidence Interval = 0.01, 0.25, p<0.001).

**Conclusion:** Self-disclosure of sensitive health information is difficult, particularly for adolescents with a stigmatized illness such as HIV/AIDS. While a number of possible factors were associated with self-disclosure of serostatus, only behavioral acquisition of HIV independently predicted willingness to self-disclose one’s status. The comparative reticence of perinatally infected youth to self-disclose may be due to several factors, but since disclosure can be an important means of gaining support and preventing secondary transmission of HIV infection, interventions should focus on helping youth, including perinatally infected youth, share their status in a way that affords them the social support and clinical benefits they need.

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*No conflict of interest*
Abstract: O_02

HIV infection and adolescents

Regimen-specific adherence to antiretroviral therapy (ART) among HIV-infected adolescents at a pediatric HIV-treatment centre in Gaborone, Botswana

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Background: With the scale-up of anti-retroviral therapy (ART), greater numbers of perinatally HIV-infected children are surviving into adolescence. Compared to younger children and adults, adolescents are known to have more poor adherence to ART. However, it is not clear if adolescents adhere better to certain types of ART regimens than others. We evaluated and compared adherence to different ART regimens among HIV-infected adolescents in Gaborone, Botswana. We further assessed the influence of age and gender on adherence to ART.

Materials and Methods: Using a case-control design, cases (adolescent visits with poor adherence: pill count < 95 >105%) and controls (adolescent visits with good adherence: 95-105%) were drawn from medical records of HIV-1 infected children receiving ART at the Botswana-Baylor Children’s Clinical Centre of Excellence, a pediatric HIV-treatment clinic in Gaborone, Botswana, between June 2003 and December 2011. Univariate and Multivariate Logistic Regression were performed to identify the independent association of ART regimen, sex and age with adherence to ART and to control for confounding, respectively.

Results: 1,962 cases and 10,158 controls were evaluated. Compared to those on LPV/r-based ART, adolescents on NVP-based ART were 25% more likely to have good adherence (OR: 1.25, CI:1.11-1.41, P< 0.001). Older adolescents (16-21 yrs) were 12% more likely to have good adherence to ART (OR: 1.12; CI:1.02-1.24, P=0.024) compared to younger adolescents (11-15yrs). There was no significant difference in adherence rates between those on EFV-based vs. LPV/r based ART. Gender was not significantly associated with adherence.

Conclusions: Our study is the largest to date to compare adherence to different ART regimens among HIV-infected adolescents in a resource-limited setting. While current World Health Organization (WHO) guidelines emphasize EFV-based regimens for initial ART in adolescents, NVP-based regimens could be considered for adolescents at perceived higher-risk of non-adherence. Likewise, LPV/r-based regimens may have wider utility in adolescent populations than current restriction to second-line ART. Younger adolescents should be followed particularly closely with respect to adherence.

No conflict of interest
Abstract: O_03

Comprehensive Pediatric HIV care

Computer-generated reminders improve quality of HIV care for pediatric patients in a resource-limited setting: A randomized, controlled trial

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Introduction: The quality of care offered to HIV-infected children in resource-limited settings is often suboptimal. We evaluated the impact of computer-generated reminders delivered to clinicians on rates of compliance with HIV care guidelines.

Methods: We conducted this randomized, controlled trial in an HIV referral clinic in Kenya caring for HIV-infected or HIV-exposed children (<14 years old). Children were randomized to an intervention group, where their clinicians received printed summaries of data in their electronic health records along with targeted reminders for overdue orders, or a control group whose clinicians received summaries without any reminders. We compared differences between the intervention and control groups in clinicians’ adherence to standard pediatric HIV care protocols, specifically HIV DNA PCR and HIV ELISA antibody testing; ordering baseline laboratory investigations, scheduled CD4 testing, and routine chest x-rays; appropriately initiating antiretroviral therapy (ART); and referring malnourished children to nutritional assistance.

Results: During the 5-month study, we enrolled 1,623 children (N=833 intervention group, N=790 control group, 49% female, 71% HIV-infected). Clinicians adhered to all care protocols three times more often for intervention patients than for controls (37% vs. 13%, p< 0.0001). Adherence was significantly greater for ordering HIV ELISA tests at 18 months of age, initiating ART for children, ordering baseline chemistries and chest x-rays, and making referrals for malnutrition. When reminders did not result in orders among the intervention group, providers gave the following reasons: test was previously ordered (35%); planned to order at next visit or other deferral (32%); disagreed or reminder not applicable (17%); or provider gave no response (16%).

Conclusions: Clinical summaries with computer-generated reminders significantly corrected overdue laboratory, imaging, and medication ordering and referral patterns for pediatric patients receiving HIV care within a resource-limited setting. This technology has broad applicability to improve quality of care in similar settings.

No conflict of interest
Abstract: O_04

Complications of HIV therapy

Vitamin D, PTH and Tenofovir Among Children/Adolescents with Perinatally Acquired HIV

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Background: HIV+ children/adolescents have high rates of Vitamin-D deficiency and are at risk for poor bone health. Tenofovir, a widely used NRTI associated with decreased bone density, was recently approved for children as young as 2 years old. Previous studies have reported elevated parathyroid hormone (PTH) levels related to tenofovir use in adults and adolescents with behaviorally acquired HIV. As part of a study of Vitamin-D supplementation in children/adolescents with perinatally acquired HIV, PTH levels in relation to Vitamin-D levels and tenofovir use was evaluated.

Material and Methods: 121 perinatally acquired HIV patients were evaluated using retrospective chart review. Among patients who did/did not receive tenofovir, Vitamin-D and PTH levels were compared using t-tests.

Results: Median age 14 years (IQR 12-18), 51% female, 77% African American. Mean CD4 817/mm3 (SD 480), mean plasma RNA 5153 cpm (SD 18661), 54% with plasma RNA <75 cpm. Mean Vitamin-D was 23.9 ng/ml with 16% Vitamin-D deficient (<20 ng/ml). 35.5% (n=43) of subjects were on tenofovir-containing regimens. Mean age of those on Tenofovir was 16.5 years (SD 3.6) versus 12.7 years (SD 4.6) for those not on Tenofovir (p < 0.001) Tenofovir use and Vitamin-D levels were not related (p > 0.2). The mean Vitamin-D levels in tenofovir users was 22.6 ng/dL (SD 13.8) compared to non-tenofovir users 24.7 ng/dL (SD 15.6) (p > 0.4). Tenofovir use was associated with higher mean PTH levels, 49.8 pg/ml (SD 33) versus 36.7 pg/ml (SD 20.2) (p<0.01). This association of elevated PTH levels in tenofovir users remained after controlling for Vitamin-D use, age, sex, race, Tanner stage and BMI in multivariate analysis (p < 0.01). PTH levels were associated with both Vitamin-D and tenofovir use in multivariate analysis. Among the 9 tenofovir users who were ≤ tanner stage 3, PTH levels remained elevated despite higher mean Vitamin-D levels of 34 ng/ml (SD 12) while PTH levels remained elevated at 48.2 pg/ml (SD 35.3).

Conclusions: Among children/adolescents with perinatally acquired HIV, tenofovir use was associated with a 35.7% increase in mean PTH levels. Of significance is the high PTH levels in younger tenofovir users despite normal mean Vitamin-D levels, raising the prospect of increased risk of impaired bone accrual in HIV infected pre-pubertal children. As tenofovir use increases in this population, further research is needed into bone health implications.

No conflict of interest
Abstract: O_05

Treatment of pediatric HIV infection

Nutritional status and other baseline predictors of mortality among HIV–infected children initiating antiretroviral therapy in Tanzania

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Introduction: Factors contributing to high mortality in the first few months after antiretroviral therapy (ART) initiation are not adequately studied among children in less developed countries. The objective of these analyses was to examine the relationships of nutritional status and other baseline characteristics in relation to mortality among children initiating ART, using routinely collected clinical data.

Materials and Methods: This was a prospective cohort study of 3144 children (age < 15 years) initiating ART between October 2004 and December 2010 in Dar es Salaam, Tanzania. The relationship between all-cause mortality and nutritional status and other baseline characteristics was examined using Cox proportional hazards model with age as the time scale.

Results: Overall, 268 (12.4%) children died over a median follow up time of 17.2 months (IQR, 4.6-31.4). After multivariate adjustment, undernutrition as measured by weight for age Z score (WAZ) was significantly associated with overall mortality. Compared with children with WAZ >-1, those with WAZ ≤-2 to <-3 had more than doubled risk of death (RR, 2.43 (95% CI, 1.02-5.78), and those with severe underweight (WAZ ≤-3), the risk more than 7-folds (RR, 7.14 (95% CI, 3.34-15.26) in this period. Other baseline risk factors for overall mortality included younger age (≤2 years), severe anemia (hemoglobin <8.5g/dL), severe immune suppression (CD4+ T-cells<15% or <200 cells/μL), history of TB, opportunistic infections, advanced WHO stage (III and IV), and ART initiation in 2007 or later.

Conclusions: Undernutrition at the time of ART initiation was associated with increased risk of death, particularly during the first three months after ART initiation. To sustain the obtained benefit of ART in this setting, interventions to improve nutritional status should be used as adjunct to ART.

No conflict of interest
Abstract: O_06

Complications of HIV therapy

Incidence of and risk factors for toxicity among HIV-infected children receiving cART: findings from a large observational cohort in western Kenya

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Introduction: Little data exists about the epidemiology of toxicity due to Antiretroviral drugs among HIV-infected children outside of controlled research settings. The objective of this analysis was to describe the incidence of and risk factors for 1) any toxicity associated with combination Antiretroviral therapy (cART), and 2) toxicity causing treatment discontinuations or regimen switches among HIV-infected children (treatment limiting toxicity).

Methods: The United States Aid for International Development-Academic Model Providing Access to Healthcare (USAID-AMPATH) Partnership is a network of 25 parent clinics and nearly 30 satellite clinics providing HIV care and treatment across a swathe of western Kenya. Since 2001, it has enrolled over 140,000 patients, including nearly 9500 HIV-infected children. Included in this analysis were confirmed HIV-positive children aged 0-13 years at enrollment, who initiated cART between 09/2002-07/2011. Incidence rates were calculated using standard epidemiologic methods. Potential risk factors and confounders considered were age, sex, concomitant administration of tuberculosis medicines and/or Cotrimoxazole, use of Stavudine and/or Nevirapine, severe immune suppression at treatment initiation, severely low height-for-age and/or weight for height, CDC (Centres for Disease Control) clinical stage at treatment initiation, and adherence to medications. We evaluated the strength of association of these variables using Cox Proportion Hazards regression modeling.

Results: There were 6084 children eligible for analysis, 51% male, 32% orphaned, median age at cART initiation of 6.0 years (IQR: 2.9 -8.7 years). Of these, 253 children reported any toxicity over the follow-up period, for an incidence rate of 1.3/1000 child-years of follow-up. There were 148 children who had to discontinue or change their regimen due to toxicity for an incidence rate of 0.8/1000 child-years. After adjustment, factors associated with an increased probability of experiencing any toxicity included age at cART initiation (Adjusted Hazard Ratio, AHR: 1.1, 95% CI: 1.0-1.2), being moderately or extremely low height for age (AHR: 3.9, 95% CI: 2.0-7.7), and being severely immune-suppressed at cART initiation (AHR: 1.8, 95% CI: 1.1-3.1). Being orphaned was associated with a reduced probability of experiencing any toxicity (AHR: 0.5, 95% CI: 0.3-0.8). Factors independently associated with an increase of treatment-limiting toxicity were having a non-biological caregiver bringing the child to clinic at enrolment (AHR: 2.4, 95% CI: 1.1-5.4), being moderately or extremely low height for age (AHR: 3.2, 95% CI: 1.2-8.3), and being severely immune-suppressed (AHR: 2.6, 95% CI: 1.2-5.8).

Conclusions: These data suggest that height for age and immune suppression are strongly associated with these children experiencing toxicity associated with cART. They also suggest a complex interplay of clinical and social factors that could be resulting in ascertainment bias, responder bias, or selection bias.

No conflict of interest
Abstract: O_07

Treatment of pediatric HIV infection

Size and Decay of the Resting CD4+ T Cell Latent HIV Reservoir During HAART in HIV-Infected Infants

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Introduction. Highly active antiretroviral therapy (HAART) within six months of HIV infection limits replication-competent HIV reservoirs in adults, but this has not been studied in HIV-infected infants.

Material & Methods. We assessed the size and decay of the resting CD4+ T cell reservoir over the first two years of life in infected infants (N=17) initiating early therapy (median age of 8.1 weeks) with lopinavir/ritonavir-based HAART who achieved adequate suppression of plasma viral load by 24 weeks.

Results. 86% of 14 infants tested at 24 weeks of HAART had a detectable latent HIV reservoir in resting CD4+ T cells at a median frequency of 1.88 [IQR: 0.24 – 3.25] infectious units per million resting CD4+ cells (IUPM). Even at 96 weeks of therapy, the resting CD4+ T cell reservoir remained measurable in 60% of 10 children retested (median IUPM =0.32). Decreasing frequencies of resting CD4+ T cells harboring replication-competent virus was observed between 24 and 96 weeks of HAART, with an estimated mean decay rate of 0.028 log_{10} IUPM per month corresponding to a half-life of 11 months [95% CI: 6 to 30 months]. Reservoir size at week 24 was correlated with time to first undetectable plasma viral load (Spearman r=0.72, P=0.004) and remained correlated through week 96 of HAART (r=0.91, P<0.001). In addition, infants initiating HAART by age 6 weeks tended to have lower reservoir size at 24 weeks of HAART (median IUPM =0.22) compared with those starting HAART after age six weeks (median age 10.5 weeks; median IUPM 3.25; P=0.071).

Conclusions. Although the latent reservoir remains detectable over the first two years of life, its size is associated with time to first undetectable viral load. To minimize HIV reservoirs in infants, rapid achievement of undetectable plasma viremia should be a therapeutic goal of HAART in infants.

No conflict of interest
Abstract: O_08

Treatment of pediatric HIV infection

Tenofovir Pharmacokinetics when Administered According to Weight Band Dosing in HIV-infected Children Receiving TDF/3TC/EFV Once Daily

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Background: Affordable once daily dosing drug such as tenofovir (TDF) is favorable for HIV-infected children and adolescents to help improve adherence and quality of life. Our objective was to evaluate the steady-state pharmacokinetics of TDF prescribed according to weight band dosing in combination with lamivudine and efavirenz in HIV-infected children.

Methods: Prospective, single arm, open label, multi-center study. HIV-infected children receiving NNRTI-based regimens, without tenofovir, aged between 3-18 years, weighing ≥15 kg, and virologically suppressed were enrolled. Their first line antiretroviral regimen was modified to a once daily regimen of TDF/lamivudine/efavirenz. TDF was prescribed according to weight band dosing with acceptable doses between 90-125% of the recommended dose (8 mg/kg for age <8 years, and 210 mg/m2 for age ≥ 8 years): 150 mg for 15-<22 kg, 225 mg for 22-<33 kg, and 300 mg for >33 kg once daily. Intensive 24-hour blood sampling for PK was performed after 4 weeks. TDF plasma concentrations were determined by HPLC and PK parameters by non-compartmental analysis.

Results: Forty HIV-infected children were enrolled: 17 (34%) were male, mean (±SD) age was 11.7 (3.5) years, and CD4 cell count was 853 (399) cells/mm³. Mean duration on HAART was 354 (155) weeks prior to enrollment. The group of children aged < 12 years of age had mean weight (±SD)23.4 (±4.8) kilograms received TDF at the mean dose of 8.1 (±1.0) mg/kg; the group aged ≥ 12 years of age had mean weight (±SD) 42.4 (±7.7) kilograms received TDF at the mean dose of 7.1 (±1.1) mg/kg. Overall, the median (range) area under curve (AUC0-24hr) was 2.64 (1.23-5.11) mg*hr/mL and C24hr was 0.05 (0.02-0.12) mg/mL. Despite of delay in Tmax, and low Cmax, the median AUC0-24hr (range) was 2.64 (1.23-5.11) µg*hr/mL which remained satisfactory. There was no significant difference in PK parameters including AUC0-24 hr, Cmax, and C24hr found between children above and below 12 years of age.

Conclusions: We demonstrate that TDF prescribed according to weight band dosing as a part of once daily antiretroviral regimen in children achieved plasma exposures comparable to studies in HIV-infected adults. The 90% confidence interval for the geometric mean AUC was within ± 20% of that reported in adults. At steady state, AUC0-24 hr and Cmax were similar to the previous studies in HIV-infected children. Although drug exposure was satisfactory, concerns remain regarding bone and kidney toxicity; long term use and risk follow-up is warrant.

No conflict of interest
Abstract: O_09

Treatment of pediatric HIV infection

IMPAACT P1066: Raltegravir (RAL) safety and efficacy in treatment experienced HIV infected (+) youth 2 to 18 years of age through week 48


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Background: New antiretrovirals are needed for HIV+ children. IMPAACT P1066 is an international Phase I/II open label multicenter trial to evaluate pharmacokinetics (PK), safety, tolerability, and efficacy of multiple RAL formulations in treatment experienced HIV+ youth

Methods: RAL was given with an optimized background regimen. Dose selection was based upon intensive PK and safety data: 400 mg BID of RAL film-coated tablet (6-18 years) and weight-based dosing (~6mg/kg BID) of a RAL chewable tablet (2 to < 12 years). Here we present demographics and 48 week safety and efficacy data in the 96 subjects who received the selected RAL dose. Subjects were stratified sequentially in 3 age cohorts (I:12-18 years; II: 6-< 12 years; III: 2-< 6 years); Cohort I enrolled first. Cohort IIA received the film-coated tablet; Cohort IIIB and III received the chewable tablet. Grade 3+ or serious adverse events (AE) were summarized. Primary virologic endpoint was vRNA < 400c/mL or ≥1 log reduction. Secondary endpoints were vRNA < 50c/mL, and change in CD4 count (%). Efficacy analyses used Observed Failure missing data approach

Results: Enrollment by Cohort was: I (N=59); IIA (N=4); IIB (N=13); III (N=20). Entry demographics were generally similar across cohorts with respect to race (54-75% Black), gender (35-75% male), with a relatively wide cohort disparity in category B/C diagnosis (23-76%). Baseline ranges across cohorts were: median CD4% (20-33) and mean HIV-RNA Log (10) copies/mL (4.3-4.4); median CD4 count declines as expected with age cohort (1087-397). At Week 48 (in all cohorts combined), RNA < 400c/mL or ≥1 log reduction was observed in 78.9%, RNA < 50c/mL in 56.7%, with a mean CD4 increase of 155.7 cells/uL (4.6%). Through Week 48, there were 15 subjects with Grade 3+ clinical AEs (1 subject with DR drug related [psychomotor hyperactivity, abnormal behavior and insomnia]); 16 subjects with Grade 3+ laboratory AEs (1 with DR AST and ALT); 14 subjects with serious clinical AEs (1 with DR rash); 2 subjects with serious laboratory AEs (1 with DR transaminase increased); no discontinuations due to AEs and no deaths.

Conclusions: Two RAL formulations were studied in HIV infected youth ages 2 to 18 years. At the selected doses, both formulations were well-tolerated and showed favorable virologic and immunologic responses through 48 weeks of treatment. Data from this study has been used in obtaining approval for these regimens in HIV+ youth in the US

No conflict of interest
Abstract: O_10

Treatment of pediatric HIV infection

Safety and efficacy of etravirine over 48 weeks in HIV-1-infected, treatment-experienced children and adolescents: the Phase II PIANO study

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Introduction: Etravirine demonstrated efficacy and safety in treatment-experienced, HIV-1-infected adults. Pediatric development is ongoing.

Materials & Methods: PIANO (TMC125-C213; NCT00665847) is a 48-week, Phase II, open-label, single-arm trial of the safety, antiviral activity and pharmacokinetics of etravirine 5.2mg/kg (maximum dose 200mg) bid in HIV-1-infected, treatment-experienced children (6–<12 years) and adolescents (12–<18 years) with screening viral load (VL) ≥500 copies/mL. All patients received an investigator-selected, optimized background regimen (OBR) of a ritonavir-boosted PI plus N(t)RTIs and optional enfuvirtide and/or raltegravir. Week 48 data are reported.

Results: Overall, 101 treatment-experienced children and adolescents were enrolled in the study, including 41 children (median [range] baseline VL 3.6 [2–7] log₁₀ copies/mL, median [range] baseline CD4 count 443 [39–1441] cells/mm³, 66% previously used 1 or 2 NNRTIs) and 60 adolescents (baseline VL 4.0 [2–6] log₁₀ copies/mL, baseline CD4 count 356 [7–1345] cells/mm³, 82% previously used 1 or 2 NNRTIs). Of the 101 patients, 63% were female and 49% white, and 76 (75%) completed the trial; most discontinuations were for adverse events (AEs) or trial non-compliance (8% each). At Week 48, 65% of patients were adherent based on a PENTA adherence questionnaire. By pill count, 39% were >95% adherent and 70% were >80% adherent. Adherence >95% was 46% for children and 35% for adolescents. The most common treatment-emergent AEs (occurring in >10% of patients overall) were upper respiratory tract infection (27%), rash (23%; grouped term), diarrhea (16%), cough (13%) and vomiting (11%). The most common AEs (occurring in >5% of patients overall) considered at least possibly related to etravirine were rash (18%; grouped term) and diarrhea (7%). Four percent discontinued due to rash. Serious AEs were seen in 5% of patients while 14% experienced a grade 3/4 AE (including two reports of grade 4 thrombocytopenia). One child had grade 3 rash maculo-papular, one had grade 3 hypersensitivity and one adolescent had grade diarrhea, all considered at least possibly related to etravirine. Laboratory toxicities were predominantly grade 1/2. At Week 48, 56% of patients (children 68%, adolescents 48%) achieved VL <50 copies/mL (intent-to-treat, non-completer=failure). Based on the intent-to-treat, time-to-loss-of-virologic-response algorithm, 53% of patients (children 68%, adolescents 43%) achieved VL <50 copies/mL at Week 48. Median time to first achieve VL <50 copies/mL was 16 weeks (children) and 24 weeks (adolescents). Forty-one patients (41%) were classed as virologic failures (VF): 29 non-responders and 12 rebounders. Of 30 VFs with available genotype at endpoint, 18 (60%) developed NNRTI resistance-associated mutations, most commonly: Y181C (n=8), E138A (n=3), L100I (n=3), and/or V90I (n=3). Mean [standard error] change from baseline in CD4 cell count at Week 48 was 156 [23] cells/mm³ (children: 178 [40] cells/mm³; adolescents: 141 [27] cells/mm³).

Conclusions: The efficacy, safety, and resistance profiles of etravirine 5.2 mg/kg bid plus OBR in this difficult-to-treat, antiretroviral-experienced pediatric population were comparable to those observed in treatment-experienced adults in the DUET trials. Response rates were better in children than adolescents, most likely due to less advanced disease status, better adherence, and less previous NNRTI use.

Conflict of interest: financial relationship(s): Gilead, Tibotec, BMS, GSK.
Abstract: O_11

Comprehensive Pediatric HIV care

Screening for Development Disabilities in HIV-Infected Children in South Africa: Results from the ASENZE Study

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Background: Despite the high rates of neurodevelopmental manifestations in children with HIV, research has been limited in this area in sub-Saharan Africa where over 90\% of the world’s HIV-infected children reside. Objectives: To compare the results of screening for risk of disability using the Ten Question questionnaire (TQ) of HIV-infected children and HIV-uninfected children and to evaluate the associations between caregiver demographics and a positive TQ.

Methods: Door-to-door population-based screening in 5 contiguous tribal peri-urban areas in KwaZulu-Natal, South Africa of all children 4-6 years old was conducted in 2008 – 2009. Community workers completed an isiZulu language TQ which evaluated the caregivers’ assessment of child’s development and behavior and scheduled a study visit during which voluntary HIV testing and neuropsychological testing was offered to children and their adult caregivers.

Results: 1787 children were screened at home by TQ and 1581 (88.5\% of eligible children) and their caregivers completed assessment and were offered HIV testing. The mother was the primary caregiver for 826 (52.2 \%), the grandmother for 280 (17.7\%), and another relative for 187 (11.8\%). Among those who underwent HIV testing, 426/1435 (29.7\%) caregivers and 65/1328 (4.9\%) of the children were HIV infected. As expected, HIV-infected children were seven times more likely to have an HIV-infected caregiver (69.2\% vs. 30.8\%, OR = 6.70 [3.91 – 11.5]). In addition, HIV infected children were less likely to have a father with an income (OR = 0.41 (0.22 - 0.75)). Overall, 45\% of the children screened positive on the TQ. Among the children that completed assessment, the frequencies of positive responses on 1, 2, 3, and >3 questions were as follows: 433 (27.4\%), 145 (9.2\%), 70 (4.4\%) and 75 (4.7\%). Prevalence of positive screening for disability by TQ (excluding caregiver questions related to vision and hearing) was higher among children with HIV (49.2\% vs. 34.4\%, OR = 1.85 (1.13-3.05)). When the combined responses to disability and behavioral questions were compared, there was a higher prevalence among children with HIV (64.6 vs. 50.0\%, OR = 1.83 (1.09-3.07)). Caregivers of HIV-infected children were more likely to provide a positive response on most of the TQ screening questions except for speech and vision. The greatest difference between HIV-infected and uninfected children was observed on the screening question for risk of motor impairment (‘Compared with other children, did your child have any serious delay in sitting, standing, or walking?’), 24.6\% vs. 7.9\%, OR = 3.82 (2.11 - 6.92), indicating an increased risk of motor impairment. There were no differences in screening results between HIV-infected and uninfected caregivers.

Conclusions: In this population-based study of pre-school aged children, the TQ screening tool identified a high prevalence of children at risk of developmental disability and impairment. HIV-infected children were more likely to screen positive on the TQ screen than uninfected children. Pending validation, this simple neurodevelopmental screening tool may be suitable for research and clinical purposes for HIV-infected children in low and middle income countries where pediatric HIV is highly prevalent.

No conflict of interest
Implementation research on PMTCT and pediatric treatment programs

Impact of the South Africa’s PMTCT Programs on Perinatal HIV Transmission: Results of the 1st Year Implementing the 2010 WHO Recommended Guidelines

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Introduction: Impact of implementing the 2010 World Health Organization’s (WHO) Prevention of Mother to Child Transmission of HIV (PMTCT) recommendations has not been assessed at population level. South Africa began implementation of the WHO PMTCT Option-A recommendation in April 2010. We assessed the impact of the first year of implementation of Option-A on perinatal MTCT measured at 4-8wks postpartum.

Material & Methods: We conducted a nationally representative, cross-sectional facility-based survey of infant-caregiver pairs attending the first immunization visit using a stratified multi-stage sampling design. Data were collected through caregiver interviews and/or from Road-to-Health cards between August 2011 and February 2012. HIV-exposed infants (HEI) were identified if their dried-blood-spot (DBS) specimens collected at 4-8wks were HIV-antibody positive. HEI’s DBS specimens were then tested for HIV infection using DNA-PCR.

Results: Of 9793 enrolled caregiver-infant pairs, 2914 (29.8%) HEI were identified. Of 2454 HEI whose mothers knew their own infection status, triple-antiretrovirals were provided to 43.8% of mothers of whom 72% with CD4 counts ≤350 cell/µl and 25.5% with CD4 counts >350 cell/µl. The unweighted and unadjusted national MTCT rate measured at 4-8wks postpartum was 3.0%. The unadjusted MTCT was similar for mixed-feeders and non-mixed-feeders (2.9% vs. 3.0%). Controlling for maternal CD4, the odds of MTCT were higher in mother-HEI pairs receiving ≤10wks of maternal-AZT and infant-NVP at birth compared with those receiving >10wks of the same regimen (AOR=2.4; 95%CI 1.1-5.5); adjusted MTCT rate was not statistically different for HEI receiving ≥4wks vs.<4wks of NVP prophylaxis (AOR=1.3; 95%CI 0.7-3.1). Adjusted MTCT rate was lower but not statistically different in mother-HEI pairs who received maternal triple-antiretrovirals than those who received >10wks of maternal-AZT and infant NVP prophylaxis at birth (AOR=0.6; 95%CI 0.3-1.5).

Conclusion: After one year implementing the 2010 WHO Option-A PMTCT recommendations, SA has decreased MTCT measured at 4-8wks postpartum to 3%. Data suggest that early antiretroviral initiation is likely to increase effectiveness. Overall MTCT and survival rates around 18-months are needed to estimate the impact of extended NVP prophylaxis during breastfeeding.

No conflict of interest
Abstract: O_13

Prevention of Mother-to-Child transmission

Preventing Postnatal HIV Transmission in Resource-limited Settings: Feasibility and Effectiveness of WHO Guidelines Option A and B at Population Level

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Introduction: Current WHO guidelines on prevention of mother-to-child transmission of HIV (PMTCT) option A recommends breastfeeding for 12 months and extended antiretroviral prophylaxis for HIV-exposed infants throughout breastfeeding period, whereas option B recommends maternal triple antiretroviral prophylaxis. This study examined and compared feasibility and effectiveness of both options in preventing postnatal HIV transmission at the population level in Zambia.

Methods: Zambia national data on PMTCT coverage for 2010 and data from field implementation of the guidelines were entered into a decision analytic model developed to estimate the overall postnatal transmission rate considering mother’s CD4 count, treatment status, access to prophylaxis, and adherence to regimens. Transmission rates were calculated based on the estimates by UNAIDS and results from HPTN046 trial.

Results: Data indicated that among 79,000 HIV-infected pregnant women, 14.9% were already on antiretroviral therapy (ART), 28% of those eligible initiated treatment, 85.9% of those not on ART received prophylaxis, 57% of exposed infants received prophylaxis, and approximately 50% adhered to extended infant prophylaxis. When applying option A, the overall postnatal transmission rate at six months was estimated as 4.00% (3,162 infections), whereas the transmission rate was estimated as 1.16% (916 infections) in the best case scenario in which full implementation of guidelines was achieved (100% access and adherence). Main bottlenecks included poor initiation of ART for eligible women, exposed infants’ poor access to prophylaxis, and misinterpretation of provisions for extended nevirapine regimen both by health workers and mothers. When option B was applied the overall transmission rate was estimated as 1.87% (1,478 infections). Sensitivity analysis further supported these findings.

Conclusions: Operational barriers and complexities of field implementations of guidelines may result in higher postnatal transmission rates than expected, especially for option A despite the theoretical comparable level of efficacy of two options. Careful consideration is required for selection of guidelines and its field implementations.

No conflict of interest
Abstract: O_14

Prevention of Mother-to-Child transmission

Lopinavir and Efavirenz Concentrations in Hair Samples as a Marker of Cumulative Exposure among Postpartum Women and Breastfeeding Infants in Uganda


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Background: As increasing numbers of African women receive antiretrovirals (ARVs) during breastfeeding, understanding kinetics of ARV transfer to infants through breast milk is critical. ARV levels in plasma or breast milk reflect exposure over short time intervals. By contrast, ARV levels in hair samples measure cumulative exposure over weeks-months and are strongly associated with outcomes in treated individuals. We measured hair concentrations of ARVs in HIV-infected mothers receiving ARVs and their infants after 12 weeks of breastfeeding in Tororo, Uganda

Methods: As part of the Prevention of Malaria and HIV disease in Tororo (PROMOTE) study, HIV-infected pregnant women were randomized to lopinavir/ritonavir-based or efavirenz-based therapy. At 12 weeks postpartum, approximately 20 strands of hair were collected from mothers and infants and ARV concentrations measured using liquid chromatography/tandem mass spectrometry. The ratios of infant: maternal concentrations were calculated for each drug and Spearman correlations between infant adverse events and hair ARV concentrations were examined.

Results: As of September 2011, 268 pregnant women had been enrolled with 259 infants born. All infants were HIV-negative at 12 weeks. We collected small hair samples from 45 mother-infant pairs on lopinavir/ritonavir and 64 on efavirenz at 12 weeks and found infant/maternal hair concentration ratios of 0.867 for lopinavir (95% CI 0.700-1.03), 0.471 for ritonavir (95% CI 0.247-0.694) and 0.396 for efavirenz (95% CI 0.303-0.488). There was no significant correlation between infant hair levels of ARVs and adverse effects.

Conclusions: We report for the first time the kinetics of ARV transfer from mother to infant during breastfeeding by assessing levels of ARVs in paired hair samples. Cumulative infant exposure to lopinavir during breastfeeding was much higher than exposure to efavirenz as assessed by hair concentrations (87% transfer versus 40%) with equal rates of protection from HIV acquisition. Further work to correlate cumulative infant exposure to ARVs via breastfeeding and toxicities is needed.

No conflict of interest
Abstract: O_15

Prevention of Mother-to-Child transmission

Neurodevelopment of HIV-exposed, but uninfected (HEU) infants at age 12-months

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Introduction: The very high prevalence of HIV among pregnant women in southern Africa results in large numbers of HIV exposed, but uninfected (HEU) children. There is growing evidence that HEU infants have increased morbidity and poor growth, but less attention has been paid to their neurodevelopment. Most studies, moreover, have failed to include an appropriate comparison group of non-exposed (NE) infants. The aim of this study was to determine if there is a difference in neurodevelopment between HEU and NE infants; and, if differences exist, whether these might be explained by maternal depression in HIV infected mothers.

Materials and Methods: HIV positive and HIV negative mothers were enrolled at delivery at three clinical sites in SW Tshwane (Pretoria), South Africa. Data were collected at birth, 3 and 12 months. A single, blinded observer performed the Bayley Scales of Infant Development, Third Edition (BSID) at 12 months. Maternal depression was measured using the Center for Epidemiologic Studies of Depression scale (CES-D). A measure of self-efficacy within the family was used to determine maternal role in raising the infant. Statistical analyses were conducted using t-test and chi-square. ANCOVA and multiple linear regression were used to control for potentially confounding variables.

Results: One hundred ninety-nine infants were enrolled in the study, 78 HEU and 121 NE. The overall average age was 377 days (HEU 372 days versus NE 381 days, p = 0.69). Maternal marital status, housing, employment and education were similar between the two groups. HEU mothers were older (28.8 vs 25.6 years, p < 0.001), more often multigravida (84.0% vs. 59.8%, p < 0.001) and had fewer adults in the home (2.63 versus 2.96, p = 0.031). Levels of depression at 12 months were similar (21.80 versus 22.74, p = 0.65), but HIV positive mothers reported higher self-efficacy (5.08 vs. 4.31, p = 0.002). At 12 months, HIV infected mothers were less likely to be breastfeeding (15.4% versus 70.2%, p < 0.001). HEU and NE infants scored similarly on both the language (91.6 versus 91.4, p = 0.33) and motor (94.5 versus 95.2, p = 0.43) components of the BSID, but HEU infants scored significantly lower on the cognitive component (94.9 versus 101.0, p = 0.004). This finding remained significant controlling for potentially confounding variables, (p = 0.003).

Conclusions: The results of this study demonstrate decreased cognitive development among HEU infants. This study was unable to determine social or maternal psychological factors that might contribute to these findings. Further investigation is required to determine possible contributing mechanisms and assess whether this finding persists over time.

No conflict of interest
Abstract: O_16

Implementation research on PMTCT and pediatric treatment programs

SAMBA - a new point-of-care test for early infant diagnosis with improved efficacy

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Introduction: Early infant diagnosis (EID) of HIV infection and initiation of antiviral treatment are critical to preventing aggressive progression of disease and high mortality in vertically infected infants. Currently, exposed infants in Sub-Saharan Africa are diagnosed by shipping dried blood spot (DBS) to centralized laboratories for molecular testing. The logistical difficulties have resulted in long turn-around time and high rates of loss-to-follow-up (LTFU) ranging from 37-83% after PCR testing. The SAMBA HIV-1 test is a simple and robust molecular test intended to provide a ‘test and treat’ approach at the point-of-care. It uses isothermal amplification with a visual readout in a closed device. Reagents are provided in unit-dose format without requiring cold chain transport. The bench-top instrument is designed to operate without sophisticated infrastructure or highly-trained personnel. This study was designed to compare the performance of SAMBA in fresh anti-coagulated whole blood from HIV infected individuals in London and in Uganda vs. DBS prepared from the same samples and tested by Roche Amplicor v1.5 (Amplicor) or COBAS AmpliPrep/Taqman (Taqman) assays.

Materials and Methods: 164 clinical samples from London UK (114 HIV positive) and 102 patients (34 HIV positive) in Arua, Uganda were tested by SAMBA using whole blood. DBS from the same samples were prepared and tested by two laboratories located in Zambia (Amplicor with manual extraction) and Uganda (Taqman with automated extraction). Discrepant samples were resolved by proviral DNA PCR and RNA quantitation by COBAS TaqMan v2 at the Royal London Hospital. Discrepant samples and 10% of concordant positives and negatives were retested by both methods. The % sensitivity and specificity were calculated. Analytical sensitivity was compared in serial dilutions of clinical samples and the WHO HIV-1 standard.

Results: SAMBA and Taqman detect both DNA and RNA, whereas Amplicor detects DNA only. In the 164 clinical samples from London, SAMBA showed 100% sensitivity (114/114) and 100% specificity (50/50) compared to 81% (92/114) and 100% (50/50) respectively by DBS with Amplicor; 86% (98/114) and 100% (50/50) respectively by DBS with Taqman. On retesting, 1 positive DBS sample became negative and 14 negatives became positive in Zambia; 3 positives became negative and 11 negatives became positive in Uganda. Of the 102 patients tested in Arua, SAMBA detected 34/34 positives compared 32/34 by DBS with Taqman. Both the two false negative DBS samples were confirmed positive by two rapid tests (Determine and Stat Pak) and proviral DNA PCR. Using dilutions of clinical samples and the WHO standard, SAMBA was 5-10 times more sensitive than DBS.

Conclusions: Compared to DBS, SAMBA showed improved sensitivity and reproducibility. The DBS results highlighted issues of sensitivity and reproducibility of the current methodology, especially when Amplicor is used in conjunction with manual extraction. As more pregnant women are put on prophylaxis treatment, the HIV level is expected to decrease in infected infants, thus a more sensitive and reproducible EID test would be required. If implemented successfully at the point-of-care, SAMBA has the potential of reducing turn-around time, LTFU and ultimately infant mortality in resource-poor settings.

Conflict of interest

financial relationship(s): CEO of Diagnostics for the Real World (DRW) with the University of Cambridge and The Wellcome Trust as corporate shareholders.
Abstract: O_17

Complications of HIV therapy

Cardiovascular structure and function in HIV-infected children in Zambia and Uganda


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Background / introduction Carotid intimal medial thickness (cIMT) and pulse wave velocity (PWV), as measures of cardiovascular structure/function, are impaired in HIV-infected UK children, although the impact of ART and obesity/lifestyle factors has been difficult to determine. No studies have been undertaken in Africa where 90% HIV-infected children live. We are undertaking a longitudinal study of arterial structure/function, nested within a large randomised trial (CHAPAS 3) of different ART regimens in Uganda/Zambia. We present baseline data on ART-naïve and ART-experienced children.

Methods All cooperative ART-naïve and experienced (stable on d4T+3TC+NNRTI for >2years) HIV-infected children recruited from 2 sites in Uganda/Zambia had baseline cIMT and PWV measurements undertaken by the same operators in each country. Differences between ART-naïve and experienced children, accounting for age and ART duration, were analysed using linear regression.

Results 180(121:59 ART-naïve: experienced) children had cIMT and 212(139:73) had PWV measured; median(range) age was 4.7(0.7-13.6 years); 53% male; median CD4% in naïve: experienced 18:33%. In ART-naïve vs experienced children, mean(sd) cIMT was 0.46(0.44)mm vs 0.47(0.35)mm (p=0.4) and PWV was 5.79(0.8) metre/second vs 5.63(0.61)metre/second (p=0.14), with a non-significant trend towards IMT and PWV increasing with age. (IMT p=0.08, PWV p=0.09) In ART-experienced children, duration of ART (median(range) 3.9(2-6.2 years)) did not influence cIMT(p=0.2) or PWV(p=0.5). Values were comparable to those of UK HIV-uninfected and lower than HIV-infected children.

Discussion In this first large study of arterial structural and function in HIV-infected children in Africa, results were similar to HIV-uninfected UK children and were unrelated to ART status. Follow-up data, comparison with African controls, and further analyses exploring the impact of lipid levels and markers of inflammation on these vascular markers may all provide insight into the pathogenesis of HIV and ART-mediated mechanisms of vascular injury and repair as well as providing guidance on optimal first-line ART for HIV-infected children in Africa.

No conflict of interest
Abstract: O_18

Preventon of Mother-to-Child transmission

Prevalence of hepatitis B virus (HBV) infection in infants born to HIV/HBV co-infected women and factors associated with vertical transmission of HBV

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Introduction: Since the integration of Hepatitis B (HB) vaccine in the Expanded Program on Immunization (EPI) in Thailand in 1992, there has been no evaluation of hepatitis B virus (HBV) transmission in infants born to mothers co-infected with HIV-1 and HBV. We assessed the prevalence of HBV infection in infants born to HIV-1 co-infected women and determined risk factors associated with transmission of HBV.

Materials & Methods: HIV-1 infected pregnant women enrolled, between 1997 and 2010, in large nation-wide trials for perinatal HIV prevention were screened for HB surface antigen (HBsAg). HBsAg-positive women were then tested for HBeAg and HBV DNA quantification. Infants born to HBsAg-positive women were tested for HBsAg and/or HBV DNA within the first 6 months of age. Factors associated with vertical transmission of HBV were analyzed using Fisher’s exact test for categorical variables and Mann–Whitney test for continuous variables. Factors included in analysis were maternal age at enrollment, alanine transaminase (ALT) level, CD4 T-cell count, HIV RNA load, HBV DNA load, HBeAg status, and infant gender.

Results: Of 3,747 HIV-infected women, 266 (7.1%) were HBsAg positive. Prior to delivery, median of maternal age was 26 years old (IQR: 22-29), ALT 17 IU/L (IQR: 12-26), CD4 T-cell count 355 cells/mL (IQR: 228-500), HIV RNA 4.02 log10 copies/mL (IQR: 3.36-4.59) and HBV DNA 4.76 log10 IU/mL (IQR: 1.84-7.70). Fifty-four percent of HBsAg positive mothers were HBeAg positive. Thirteen of 251 evaluable children (5.2%; 95%CI 2.8-8.7) were infected with HBV. Ten infants were born to HBeAg-positive mothers, of whom, six were found to be infected at birth and were born to women with HBV DNA >7 log10 IU/mL. Three were born to HBeAg-negative women. None of the HBV infected infants were HIV infected. Women who transmitted HBV to their infants had higher median ALT level, as compared to non-transmitters (25 vs. 17 IU/L, p=0.02). High HBV DNA level and HBeAg positivity were associated with HBV transmission (p=0.056 and 0.096, respectively).

Conclusions: The prevalence of HBV infection in infants born to HBV-HIV-1 co-infected women was 5%. Maternal factors potentially associated with the risk of HBV vertical transmission were elevated ALT, HBV DNA levels, and HBeAg positivity. In addition to infant HB vaccination, other interventions targeting women with high HBV DNA or HBeAg positive are thus needed to further decrease transmission of HBV.

No conflict of interest
Abstract: O_19

Complications of HIV therapy

Immunity to Measles, Mumps and Rubella Among School-Aged Perinatally HIV-Infected U.S. Children and Youth


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Introduction: There is concern that perinatally HIV-infected (PHIV) youth who received measles-mumps-rubella (MMR) vaccine(s) prior to effective highly active antiretroviral therapy (HAART) may not be adequately protected against these preventable and potentially serious viral infections.

Materials & Methods: Measles, mumps and rubella antibody levels were measured by enzyme-linked immunoassay (EIA) in serum obtained from Pediatric HIV AIDS Cohort study (PHACS), a multi-site, prospective cohort study of PHIV and HIV-exposed but uninfected (HEU) participants in the US and Puerto Rico. Demographic and clinical characteristics for PHIV and HEU participants were summarized. Seropositivity, as a marker of immunity, was defined as an EIA antibody index value ≥ 1.10 for measles, detectable EIA antibody for mumps, and an EIA antibody index value ≥ 1.10 (≥ 10 IU/mL) for rubella. Prevalence of seropositivity to each antigen was calculated with 95% confidence interval (CI) separately for PHIV and HEU children; prevalences of seropositivity in PHIV and HEU for each antigen were compared using the chi-squared test.

Results: For PHIV (n = 428) and HEU (n = 221) participants (at the time of blood collection) mean (range) ages were 14.5 (7.6-19.8) and 12.5 (7.5-19) years, females comprised 54% and 48%, race was black in 75% and 64%, at least one MMR dose was documented in 98% and 92%, and at least two MMR doses in 91% and 75%, respectively. For PHIV children, 93% were on antiretroviral therapy, mean (range) CD4 count and percentage were 754 (11-2,330) cells/µL and 32% (1%-59%), and 68% had viral load < 400 copies/mL. Prevalences (95% CIs) of seropositivity were significantly lower among PHIV than HEU participants: 46% (41%, 51%) vs 98% (95%, 99%) for measles; 59% (55%, 64%) vs 97% (94%, 99%) for mumps; and 65% (61%, 70%) vs 98% (95%, 99%) for rubella (p < 0.001 for all comparisons). Among PHIV participants with viral load < 400 copies/mL at serologic testing, 71%, 69% and 69% were seropositive for measles, mumps, and rubella, respectively. Among PHIV participants with CD4 count ≥ 500 cells/mm³ at serologic testing, 78%, 78% and 76% were seropositive for measles, mumps, and rubella, respectively.

Conclusions: Low measles, mumps and rubella seroprevalences in school-aged PHIV children (compared to HEU children)— including in those with evidence (CD4 count, viral load) of well controlled HIV infection – indicate that PHIV children in the US may be at increased risk of developing measles, mumps and rubella. New strategies should be considered to improve protection of this vulnerable population against these potentially serious viral infections.

No conflict of interest
Abstract: O_20

Complications of HIV therapy

Lipid profile in children randomized to immediate versus deferred nevirapine-based antiretroviral therapy in the PREDICT study

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Background: Lipid abnormality is a common long-term complication in HIV-infected children. This study aimed to compare lipid profiles in children randomized to immediate versus deferred nevirapine-based antiretroviral therapy (ART).

Methods: This was a substudy of PREDICT (NCT00234091), a 144-week randomized trial of immediate ART (at CD4 15-24%) versus deferred ART (at CD4 < 15%) in ART-naive Thai and Cambodian children 1-12 years of age with baseline CD4 between 15-24%. Fasting lipid profile was compared between arms. Statistical analysis was done using Paired t-test or Wilcoxon singed-rank test where appropriate. Random effects model was used for multivariate analysis.

Result: Data from 129 immediate arm and 134 deferred arm children were included. The median (IQR) age was 6.5 (4.1-8.5) years, 42% were male and 57% were Thai. Median fasting time was 8 hours. Parameters did not differ significantly between arms at week 0. By week 144, 60 deferred arm children had started ART.

Dyslipidemia was significantly less common in the immediate arm. The immediate arm had significantly higher total cholesterol (TC), low-density lipoprotein (LDL), and high density lipoprotein (HDL) but lower triglyceride and TC/HDL ratio than the deferred arm. By multivariate analysis, the mean differences over 144 weeks between the immediate arm versus the deferred arm without ART (n=73) were significant for all lipid parameters: TC (20.2, p < 0.001), triglyceride (-9.8, p = 0.006), LDL (9.1, p < 0.001) and HDL (13.0, p < 0.001) whereas only HDL was significantly different when the immediate arm were compared to the deferred arm children with ART (n=61) (4.9, p 0.001).

Conclusions: After 3 years, children randomized to immediate nevirapine-based ART had less dyslipidemia and lower TC/HDL ratio than the deferred ART group. This supports earlier nevirapine-based initiation to achieve favorable lipid profile in children with mild to moderate HIV-associated immune deficiency.

No conflict of interest

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Abstract: LB_01

Evidence of Coronary Vessel Wall Thickening in Asymptomatic Young HIV Positive Patients Using MR Imaging of HIV-associated Vasculopathy


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Background: HIV-infected patients demonstrate premature and more severe vasculopathy relative to controls. Therefore, development of a reproducible vascular imaging biomarker in this population is important. The purpose of this study was to assess coronary artery wall thickness in patients who acquired HIV in early life compared to healthy controls using a novel black-blood coronary vessel wall MR imaging technique.

Materials and Methods: We prospectively studied 20 young HIV-infected adults and 12 HIV-uninfected control subjects. Participants were free of known active cardiovascular disease or symptoms at the time of the scan. MR imaging of the proximal right coronary artery (RCA) wall was performed using phase-sensitive dual inversion-recovery black-blood vessel wall imaging. Group comparisons were performed to evaluate differences in proximal RCA wall thickness and potential associations between clinical variables and wall thickness were evaluated using linear regression analyses.

Results: HIV-infected subjects ranged in age from 15-29 years, with an average age of 21.1 years (50% male). The average RCA wall was significantly thicker in HIV-infected patients compared to controls (p-value=0.0015), despite the fact that controls were significantly older (p=0.0001). In HIV-infected subjects, linear regression analysis did not show significant correlation between the RCA wall thickness and duration of disease, current or nadir CD4 counts, levels of total cholesterol, LDL cholesterol, or triglycerides.

Conclusion: We have demonstrated statistically significant increased proximal RCA wall thickness as a likely surrogate marker of generalized vascular disease in a group of young patients who acquired HIV in early life compared to HIV-uninfected subjects. Although we did not find a significant correlation between the vessel wall thickness and markers of infection such as CD4 counts, we believe studying a larger sample size is warranted to determine more definitively if such a correlation exists.
Therapeutic DNA vaccination in HIV-infected children and adolescents: 96 weeks data from the PEDVAC Trial.

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Background: The PEDVAC study is the first trial to analyze the feasibility of a therapeutic vaccination strategy with a DNA-HIV vaccine (HIVIS) in infected children.

Materials and Methods: The HIVIS is a combination of seven plasmid DNA constructs, expressing nine different HIV-1 genes, intramuscularly delivered as two entities—one containing the gag p37 (BA and B) and RT genes and the other containing gp160 (A, B, and C) and rev genes—to minimize interference between antigens. Twenty vertically HIV-1 infected children (4-16 years of age) on stable viral control for at least 6 months (HIV-1 RNA <50 copies/ml) and CD4+ value above 400 cells/mm3 or 25% over 12 months of follow-up, were recruited into a randomised Phase II study. Ten children continued their previous antiviral regimen (arm A) and ten children were intramuscularly immunized with the HIVIS in addition to their HAART regimen (arm B). Immunization took place at week 0, 4 and 12 and with a boosting dose at week 36.

Results. Cellular immune reactivities to full MN viral antigens, to recombinant gag p24 and to purified env and RT were monitored by lymphocyte proliferation assays and intracellular staining. At week 16, four vaccinated but no control child strongly responded to the HIV MN antigen with a Stimulation Index (SI) level over 15 (p 0.087). Six vaccinated children had increased their reactivity to MN SI over 3.

Immunogenicity to gag was confirmed, since the total highly elevated SI values to p24 for week 12-72 tended to be higher in the vaccinated compared to the non-vaccinated group (p 0.058). The SI levels for RT were elevated in four vaccinated individuals at visit 12 and thereafter in seven vaccinated individuals over time, compared to one (p 0.025) and none (p 0.007) of the controls respectively. Env antigen did not give rise to cellular immune responses, and neither antigen gave rise to specific antibodies. At visit 16, the frequency of HIV-specific CD8+ lymphocytes releasing perforin (>0.200%) was higher in vaccinated than non-vaccinated children (p 0.030). At that time none of the non-vaccinated children had levels of CD8+ lymphocytes releasing perforin exceeding that level, confirming that this was the immunologically most activate time point. IFN-gamma-positive CD8+ lymphocytes as well as IFN-gamma-positive or IL-2-positive CD4+ lymphocytes did not differ significantly between the two groups.

Safety data showed good tolerance to the vaccinations. None had a decrease in CD4+ lymphocyte cell counts from baseline. Four children, two per arm, experienced a single viral blip (all four not exceeding 1000 HIV-RNA copies/ml) that returned under 50 copies/ml the following determination. No significant differences between the two arms were observed in ultrasensitive HIV-RNA viral load at week 16 and 40, and HIV-DNA at week 0, 48 and 108.

Conclusions: This first attempt to study therapeutic HIV-DNA immunizations in perinatally HIV-infected children showed that the tested regime was feasible and safe. Further studies including larger number of children and with longer follow-up are needed to clarify the clinical role of this therapeutic strategy on the management of HIV-infected children.
Pharmacokinetics and acceptability of a new generic lopinavir/ritonavir sprinkle formulation compared with syrup/tablets in African, HIV-infected infants and children according to WHO weight-band dose recommendations (CHAPAS-2)


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Background: Lopinavir/ritonavir (LPV/r) formulations for infants/children remain challenging, particularly in resource-limited settings. In the CHAPAS-2 trial, we evaluated the pharmacokinetics (PK) and acceptability of a new sprinkle formulation (40/10 mg per delivery capsule, Cipla Pharmaceuticals) versus innovator syrup or Cipla paediatric tablets (100/25 mg) in HIV-infected Ugandan children.

Methods: Randomised cross-over PK study-1 compared (twice-daily) BD sprinkles versus tablets in 24 children (4-13 years, <25 kg); PK study-2 compared BD sprinkles with syrup in 16 infants (3-<12 months), 12-hour intensive PK plasma sampling 0, 1, 2, 4, 6, 8, 12 hours after observed intake of lopinavir/ritonavir+2 NRTIs with food was performed 4 weeks post-randomisation to tablets/spinkles (Study-1) or syrup (Study-2) following WHO 2010 dosing. Children then switched to the alternate formulation and PK sampling was repeated at week 8. Lopinavir concentrations in plasma were determined using high-performance liquid chromatography. Area-under-the-curve (AUC0-12h), maximum concentration (Cmax) and concentration 12 hours post dose (C12h) are presented as geometric means (GM), within-child GM ratios (GMR) with confidence intervals (CI). Acceptability data were collected from questionnaires administered at weeks 0, 4, 8, 12. At week 8, children/carers choose which formulation to continue.

Results: Study-1 enrolled 29 children (median (IQR) age, 6.2 (5.7-8.0) years); 13 (45%) were boys. Study-2 enrolled 14 infants (age 0.5 (0.4-0.6) years); 6 (43%) were boys. 2 (5%) were ART naïve. Among 80 PK profiles, 25 and 11 in Study-1 and Study-2 were compared within-child, respectively. The GM (95%CI) AUC0-12h was 83.1 (66.7-103.5) and 115.6 (103.0-129.8) h mg/L with coefficient of variation (CV%) of 49% and 29% for sprinkles versus tablets; GMR (90%CI) was 0.72 (0.60-0.86). For sprinkles versus syrup, GM (95%CI) AUC0-12h was 70.9 (41.8-120.2) and 62.5 (35.6-109.7) h mg/L with CV% of 62% and 66%; GMR (90%CI) was 1.13 (0.62-2.06). Subtherapeutic levels (<1.0 mg/L) occurred in 4 (16%)/1 (4%) sprinkles/tablets, (p=0.35 exact) and 0 (0%)/3 (27%) sprinkles/syrup, (p=0.21). The most common food caregivers gave sprinkles with was porridge (29%) and honey (17%); in Study-2 83% of infants were breastfed. Taste was the most problematic characteristic reported in 40% sprinkles versus 0% tablets (Study-1) and 47% sprinkles versus 47% syrups (Study-2). Swallowing was problematic in 7% sprinkles versus 10% tablets (Study-1) and 13% sprinkles versus 53% syrups (Study-2). Storage, transport and conspicuousness were less problematic for sprinkles compared with syrups. Several caregivers commented about the number of capsules needing to be opened for the older children. At baseline 41% of caregivers in Study-1 and 50% of caregivers in Study-2 thought they would prefer sprinkles; at 12 weeks 20% and 67% actually reported preferring sprinkles. At week 8, 10/14 (71%) caregivers in Study-2 chose to continue sprinkles rather than syrups; in Study-1, only 7/29 (24%) children (five <6 years) chose sprinkles.

Conclusions: Exposure to LPV/r from sprinkles was comparable with syrup in infants but was lower than tablets in older children. Variability was high with both sprinkles and syrup, with no significant subtherapeutic concentrations between formulations. Sprinkles were more acceptable than syrups for infants, but for older children, who could already swallow tablets, the taste of sprinkles was of particular concern. Cross-over Study-3 comparing syrups to sprinkle in 1-4 year-olds is ongoing.
4th International Workshop on HIV Pediatrics

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ABSTRACTS

Poster presentations
Abstract: P_01

HIV infection and adolescents

Clinicians underestimate sexual risk behaviour in female patients with perinatally acquired human immunodeficiency virus infection. ANRS Co19 Coverte.

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Background: HAART has allowed children infected with HIV at birth to reach adulthood. A few published studies suggest that sexual behaviour was similar in HIV-infected and uninfected youths. Clinicians should play a key role in preventing HIV transmission in these youths. We compared patients’ reports and clinicians’ perceptions of sexual behaviours.

Methods: HIV-infected youths, aged 18-25 and diagnosed before the age of 13, have been enrolled since 2010 in the French multicenter ongoing ANRS CO19 COVERTE cohort. Each year, sociodemographic characteristics, tobacco/alcohol use and sexual behaviour are recorded in questionnaires completed by clinicians and patients. We compared the responses given by patients and clinicians, using the κ-coefficient and the McNemar-χ-square test. We investigated the factors associated with discordance on condom use between clinicians’ and patients’ reports.

Results: Among the first 97 youths included in COVERTE (most perinatally infected) at a median age of 21 years (IQR: 19-24), 58% were girls, 88% were French, 52% were living with their family, 82% had completed high school; 31% had a detectable viral load at last evaluation. Sexual experience was reported by 77% (75/97) of patients, with a median age at first intercourse of 17 years (16-18). All patients but one reported condom use at first intercourse. Clinicians’ and patients’ reports were largely consistent for socio-demographic characteristics, tobacco/alcohol use, lifetime sexual activity (all κ ≥ 0.70), age at first intercourse (κ = 0.85) and contraceptive pill use (κ = 0.70). However, inconsistent condom use in the last year, in sexually active patients, was reported in 13% of cases by clinicians (15% in boys, 11% in girls) and in 45% by the patients (respectively 14% and 59%) (κ = 0.26). This discordance was more frequent for girls than for boys (44 vs 5%, p=0.003), and for patients who reached high-school diploma or a lower level compared to those with a higher level (41% vs 0%, p=0.003). Among patients with detectable viral load at the last visit, none of the boys but 45% of the girls reported inconsistent use of condom in the last year.

Conclusion: Age at first intercourse was similar in patients HIV infected since childhood and in the French general population. Half of the sexually active girls reported inconsistent or no condom use in the last year. Clinicians were aware of patients’ sexual activity, but strongly underestimated at-risk sexual behaviour in girls and in those with medium and low levels of education. Active counselling could be actively recommended for these groups.

No conflict of interest

Abstract: P_02

HIV infection and adolescents

A First Look at Open Label Use of Pre-Exposure Prophylaxis among Young Men Who Have Sex with Men (YMSM)

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Abstract: P_03

HPV & STI Screening in Adolescent Males With HIV Engaged in Care

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Introduction: Human Papillomavirus (HPV) infection is found to be more prevalent in HIV-infected than uninfected men (73% v43%). YMSM with HIV with HPV anal lesions often deny or are unaware of these lesions. Unless screened, these lesions will remain undiagnosed with a potential for transmission to sexual partners and progression to fistula, dysplasia or cancer. We explored screening practices for HPV and therapeutic/diagnostic outcome of HPV screening among young HIV+ MSMs. We also explored whether these YMSM were co-infection with other STIs.

Materials & Methods: Examination and chart review of all HIV+ adolescent males, age 13-24 years, reporting MSM, engaged in care, 2007-2009, at an inner city HIV clinic for adolescents and young adults.

Results: The average number of males enrolled in care was 143 per year (range 127-166). By visual inspection (without use of acetic acid) 50 males were identified with anal HPV lesions. Of these 50 YMSM: 46% received anal cytology, 30% were identified as abnormal (ASCUS, LGSIL, or HGSIL); 45% received medical treatment (Imiquimod or Podophylline); 80% with
Conclusions: Detecting genital warts by visual inspection without acetic acid is an insensitive screening, thus the number of males suspected to have HPV would be higher than the 50 identified by visual inspection. In this cohort of HIV+ YMSM with HPV, a third were identified as having abnormal cytology, which is worrisome for infection with oncogenic HPV subtypes. Not all received HPV medical and or referred for surgical treatment. There is no currently approved test to detect HPV in men, however, clinicians should routinely screen all HIV+ YMSM by visual inspection of genital and anal areas with acetic acid and anal cytology as the prevalence of infection and consequent anal dysplasia appears to be high. Further, secondary risk reduction prevention strategies (including condom use) need to be discussed as these YMSM were co-infected with other STIs.

No conflict of interest

Abstract: P_04

HIV infection and adolescents

Impact of antiretroviral therapy on quality of life in HIV-infected children with moderate immune deficiency; week 144 results from PREDICT


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Background: The effect of antiretroviral therapy (ART) timing on quality of life (QOL) of HIV-infected children is understudied.

Methods: 299 HIV-infected children ages 1-12 year-old with moderate immune deficiency (CD4 15%-24%) from Thailand and Cambodia were randomized to immediate-arm (started ART at week 0, N=149) vs. deferred-arm (started ART when a confirmed CD4 was <15%, N=150) in the PREDICT study. Primary caregivers completed age-specific Pediatric AIDS Clinical Trials Group QOL questionnaires at week 0 and every 24 weeks until 144 weeks.

Results: Mean (SD) age of children was 6.3 (2.8) years, 58% were female, 60% were Thai, CD4 percentage was 20% (4.6), %CDC clinical category N:A:B was 2:62:36. 29% knew their HIV status. QOL scores between arms were not significantly different at baseline and at week 144 (all p>0.05). Within the deferred-arm, QOL scores were similar regardless of ART status (46% initiated ART). However, when compared QOL score between week 144 and baseline, immediate-arm had significant increased QOL scores in 6 domains (health perception, physical resilience, physical functioning, psychosocial well-being, health care utilization, and symptoms; p<0.01), deferred-arm had significant increased QOL scores in 4 domains (health perception, physical functioning, health care utilization, and symptoms; p<0.01). By multivariate random effect linear regression analysis of QOL score change overtime (adjusted for age, gender, race, HIV-disclosure status, and baseline QOL score), immediate-arm had associated with higher QOL score changes in 3 domains; health perception (p=0.02) and physical resilience (p=0.01), and symptoms (p=0.02) compared to deferred-arm.

Conclusion: QOL scores were similar among children in the immediate and deferred arms at week 144. However, immediate-arm children had improvement in QOL scores in 3 domains compared to deferred-arm. This improvement could be from the effect of earlier treatment on
child’s health or parents’ perception of more physical health issues in untreated children.

No conflict of interest

**Abstract: P_05**

**HIV infection and adolescents**

**Using Technology to Retain Young MSM in an Open Label Pre-Exposure Prophylaxis Study**

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**Background:** Retaining youth participants in HIV-prevention trials presents unique challenges. Factors related to social instability (e.g., poverty, housing status) influence participant interest and attendance, thus are barriers to consistent data collection. This paper explores challenges and strategies for retaining HIV negative youth in a pre-exposure prophylaxis (PrEP) trial.

**Methods:** Data were derived from a cohort of young men who have sex with other men (YMSM) participating in the open label extension of the Pre-Exposure Prophylaxis Initiative (iPrEx OLE) at the CORE Center in Chicago, Illinois. Variables including housing status, frequency of contact prior to study visits, number of missed visits, and primary method of contact (phone, text message, email, and Facebook) were Abstracted from locator forms, progress notes, and study visit forms.

**Results:** Forty-three participants (mean age = 21; 56% AA, 35% Latino) have been enrolled thus far. Twelve percent of participants listed a youth shelter as their permanent address. In the first 12 weeks of the study, 30.2% of the participants changed their address at least once and 46.5% changed phone numbers. In contrast, 93% had no change in their main social networking profile, Facebook. 132 communication exchanges took place between study staff and participants prior to their Week 4 visit; 124 exchanges were needed to assure Week 8 data collection (after initial contact, 46% via text); 122 exchanges were needed for Week 12 visits (after initial contact, 51% via text). This intensive level of follow-up led to high retention rates ranging from 80-93% across the first 12 weeks of the study. Text messages appeared to be the most effective method for communicating with participants and ensuring study visit attendance.

**Conclusions:** Multiple modes of frequent contact from study staff are necessary to maintain high study visit attendance with youth. Text messaging appears more acceptable than phone calls, while Facebook is particularly effective when participants have inconsistent phone service. Researchers must stay current with popular methods of communication among youth and ensure frequent updates to locator information. Maximizing retention methods for YMSM in PrEP trials can help inform PrEP implementation down the road.

No conflict of interest

**Abstract: P_06**

**HIV infection and adolescents**

**Factors Affecting Acceptance of the Routine HIV Screening of Adolescents in Pediatric Emergency Departments**


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**Introduction:** In 2006 the U.S. Centers for Disease Control and Prevention called for
universal opt-out HIV screening in healthcare settings including Emergency Departments (EDs). In 2011 the American Academy of Pediatrics also endorsed routine HIV screening among adolescents. The data on HIV screening in pediatric EDs are limited. This study aimed to investigate the acceptance of rapid oral fluid HIV screening among adolescents in pediatric EDs.

Methods: A prospective, cross-sectional study of patients ≥13 years in two pediatric EDs of Washington, District of Columbia (DC) was conducted over 24 months. Data on patient demographics and reasons or opting-out of screening was collected. Logistic regression was used to identify actors associated with acceptance of HIV screening.

Results: A total of 8,540 HIV tests were offered, 6,084 (72%) adolescents did not opt-out, and of those 5,669 (93%) were screened. The most common reasons adolescents cited for opting-out of testing included a prior negative test (35%; n=816) and reporting being not at risk (15%; n=353). The majority of patients screened were black (81%), female (58%), the median age was 16 yrs, and 68% were DC residents. Younger adolescents (13-14 yrs) were significantly more likely to opt-out of testing than older adolescents (OR: 1.71; 95% CI: 1.35-2.16). DC residents were significantly less likely to opt-out of the HIV screening compared to non-DC residents (OR=0.86; 95% CI: 0.77-0.96).

Conclusions: The majority of adolescents accepted routine oral fluid rapid HIV screening in pediatric EDs. Older adolescents (≥15 yrs old) were more likely to accept HIV screening. Adolescents residing in an area of high HIV prevalence (DC) were more likely to accept the HIV screening than adolescents from lower prevalence areas. Further studies are necessary to evaluate the factors affecting acceptance of routine pediatric ED HIV screening by adolescents.

No conflict of interest

Abstract: P_07

HIV infection and adolescents

Comparison of video-based HIV counseling to written HIV information in offering HIV testing to adolescent patients in an urban emergency department

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Introduction: In 2010, the New York State Department of Health reduced the amount of HIV counseling required to obtain informed consent for HIV testing to a list of 7 information points. This study compared the effectiveness of a brief, theory-based, youth-friendly HIV counseling video to this written HIV information in conveying HIV knowledge, obtaining agreement for HIV testing, and reducing risk behavior among urban adolescents.

Methods: A two group randomized controlled trial was conducted on a convenience sample of 256 non-critically ill, sexually active individuals aged 15-21 in an urban emergency department. Participants in the control group received written HIV information while those in the intervention (video) group watched a series of pre- and post-test counseling videos tailored to patients’ Stage of Change. All participants completed pre- and post-intervention measures on HIV knowledge and three mediating variables hypothesized to reduce unsafe sexual behavior: condom intention, condom outcome expectancy, and condom self-efficacy.

Results: 256 patients were enrolled and randomized, 129 in the video group and 127 in the written information group. The groups were similar with respect to age, gender, race, ethnicity, and sexual history. Acceptance of HIV testing in the video group was similar to that in the control group (85% vs. 91%, p=.20). Youth randomized to the video intervention group showed more improvement than those in the
control group on HIV knowledge (beta=.41, 95% CI=.09, .74, p=.01), female condom outcome expectancy (beta=.13, 95% CI=.04, .23, p=.01), and intention to use condom during vaginal sex (beta=.37, 95% CI=.17, .58, p<.0001).

Conclusions: Both written information and the counseling video obtained high rates of acceptance to HIV testing. However, the use of a theory-based, youth-friendly video improved teens’ knowledge and behavioral intentions more than written HIV information measured immediately following the intervention. Longitudinal studies are needed to evaluate the sustainability of these effects.

No conflict of interest

Abstract: P_08

HIV infection and adolescents

HIV infection among older children and adolescents in the IeDEA Central African region

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Introduction: Over half of vertically HIV-infected children die before 2 years of age in sub-Saharan Africa, and until recently it was assumed that few survived past 5 years. However evidence has emerged demonstrating a substantial HIV epidemic among older children and adolescents in countries with long-standing generalized HIV epidemics, where availability of PMTCT services has been limited. HIV infection in older children and adolescents is not well characterized as compared to adults. Due to regional instability and relatively poor infrastructure there is a particular dearth of data on HIV infection among older children in Central Africa.

Materials & Methods: We evaluated the overall health, and likelihood of vertically-acquired infection, among 412 HIV-infected older children aged 2-18 years attending four HIV care programs in Burundi, Cameroon and Democratic Republic of Congo from 2008-2011, as part of the Central Africa region International Epidemiologic Databases to Evaluate AIDS (IeDEA).

Results: Age distribution was: 25% 2-4 years; 41% 5-9 years; 34% 10-18 years. Gender distribution was fairly equal (51% male, 49% female). The majority of children were diagnosed at voluntary counseling and testing facilities (53%), with 30% being diagnosed at a reference hospital and 9% at a district hospital. Just 2% were diagnosed through PMTCT programs. Less than half (46%) knew their HIV serostatus, and 57% had initiated anti-retroviral therapy (ART). Reported adherence to ART was 90%. Health problems upon physical examination were common among all children, though significantly more so among those ART-naïve vs ART-initiated. Problems included skin conditions (33% vs 15%, p< 0.001), abnormal sensory system (24% vs 8%, p< 0.001), presence of ganglions (24% vs 2%, p< 0.001), abnormal thorax (17% vs 6%, p< 0.001) and abdominal conditions (13% vs 4%, p=0.001). At baseline nearly half of children (47%) were at WHO clinical stage III. As compared to those ART-naïve, having initiated ART was significantly associated with being clinical stage III (p=0.01), but was not associated with other clinical staging groups. 14.4% of children were experiencing signs or symptoms of tuberculosis, and 3% were currently taking anti-tuberculosis treatment. Signs/symptoms of tuberculosis were significantly more common among those ART-naïve (p<0.001).Data suggested vertically-acquired infection was likely in most children. Just one participant reported ever having sex, 20% had a transfusion, and only 5% of mothers received PMTCT (18% were unknown). Of 277 children with known maternal status, 28% of mothers were deceased. Stunting defined as a z score=-2, associated with long-term HIV survival, was apparent in 42% of children.
**Conclusions:** Access to PMTCT in Central Africa lags behind other African regions, yet few data are available on HIV infection among older children. Findings from this research suggest a high burden of HIV-related health problems among older children and adolescents receiving care in this setting, many of whom may have acquired HIV vertically. Significant barriers exist in access to HIV testing for older children and adolescents, and subsequent HIV prevention and care services. HIV programming in Central Africa must address the needs of older children, while increasing access to PMTCT services.

No conflict of interest

**Abstract: P_09**

**HIV infection and adolescents**

**Predictors of Substance Use Initiation among Perinatally HIV-infected and Exposed but Uninfected Children**

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**Introduction:** Experimentation with substances increases in adolescence, and risk factors are multifactorial. Risks for children affected by HIV, both perinatally infected (PHIV+) and those perinatally exposed but uninfected (PHEU), are not well-understood, and may be influenced by factors related to HIV or the family environment. This is one of the few studies to examine prevalence, incidence and predictors of substance use (SU) in a multi-site cohort of PHIV+ and PHEU youth from similar sociodemographic environments.

**Methods:** Participants included PHIV+ and PHEU youth, ages 10-16 years at baseline, enrolled in the Adolescent Master Protocol (AMP), a US-based study examining the impact of HIV and antiretroviral therapy on youth. SU data was collected by audio computer assisted self-interview (ACASI); demographic information was obtained from face-to-face interviews with youth and caregivers. Cox proportional hazards models were used to identify risk factors for initiating marijuana, alcohol, or cigarette use.

**Results:** 354 PHIV+ and 157 PHEU youth were included (50% female; 72% black; 29% Hispanic). PHIV+ and PHEU youth reported similar prevalence of marijuana, alcohol and cigarette use by age. Their prevalence was also similar to that for youth in nationwide surveys. Girls were less likely than boys to initiate marijuana (adjusted hazard ratio [aHR]=0.65; 95% CI=0.45, 0.95; p=0.03) and alcohol use (aHR=0.75; 95% CI=0.53, 1.06; p=0.11). Children living with a non-relative were less likely to initiate marijuana (aHR=0.64; 95% CI=0.38, 1.09; p=0.10) and alcohol use (aHR=0.40; 95% CI=0.24, 0.8; p<0.001). None of the covariates examined were statistically associated with initiation of cigarette use.

**Conclusions:** Children affected by HIV report similar prevalence of SU to that reported in nationally representative samples. Factors related to gender and the family context may influence the likelihood that a child affected by HIV will initiate SU; however HIV status was not statistically associated with SU risk.

No conflict of interest
Abstract: P_10

HIV infection and adolescents

Substance use self-report by adolescents with HIV: How valid is it?


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Introduction: Substance use by youth living with HIV (YLH) is a significant concern due to potential interactions between virus effects on immunity as well as potential adverse effects on risk behaviors, neurocognition, and medication adherence. In research with YLH, self-report measures of substance use are cost-effective and efficient assessments of risk behaviors. This analysis reports data from a sample of YLH who were co-enrolled in a study of neurocognition that collected substance use by self-report and a treatment study from which samples were available to assess blood toxicology assays. Toxicology results were compared to self-report. The purpose of the analyses was both to describe substance use among YLH and to examine agreement between toxicology assays and self-report of substance use in youth enrolled in research studies.

Material and Methods: Seventy-eight youth age 18-24 with behaviorally acquired HIV (80% male, 69% African American) completed an audio computer-assisted self interview version of the Alcohol, Smoking, and Substance Involvement Screening Test (ASSIST) as part of their participation in Adolescent Trials Network for HIV/AIDS Research multicenter protocols conducted at 20 sites across the U.S. Fifty-seven uninfected youth, matched for age, gender, and race/ethnicity, completed a pencil-and-paper version of the measure. Both versions assessed frequency of use of nine classes of drugs of abuse, including tobacco and alcohol, over the three months preceding the visit. Elisa-based toxicology assays tested for the presence of 27 substances in plasma. Chi-square tests were used to compare substance use between YLH and uninfected youth and Kappa statistics compared agreement between self-report and toxicology.

Results: Positive self-report among YLH was 49% for marijuana, 56% for tobacco, and 87% for alcohol, with 20%, 28% and 4% reporting daily use for each substance, respectively. The uninfected youth reported similar substance use patterns despite use of a different reporting methodology. Use of other substances was uncommon in either group by both self-report and toxicology. While half-life of individual metabolites varied greatly, 100% of youth who reported daily use of either marijuana or tobacco had positive toxicology screens; concordance decreased with less frequent self-reported use, as expected. For youth who denied use of cannabis, 7% of YLH and 6% of uninfected youth tested positive, and for youth who denied use of tobacco, 18% of YLH tested positive.

Conclusions: YLH report high rates of marijuana, tobacco, and alcohol use but low rates for other substances. Overall, substance use patterns are similar between YLH and matched, uninfected youth. Agreement between self-report and toxicology is high for marijuana and tobacco use in both subject groups, particularly for daily users, the youth of greatest concern. Results indicate that self-report can be used as a valid indicator of substance use in research studies of late adolescents and emerging adults with HIV.

No conflict of interest
Abstract: P_11

HIV infection and adolescents

Association of APOBEC3G and CD4 decline in Thai and Cambodian HIV-infected children with moderate immune deficiency

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Introduction: Human APOBEC3G is a host defense cellular factor that inhibits HIV replication. It has been reported that a genetic variant of APOBEC3G; H186 in GG, was associated with decline in CD4 T cells and higher HIV-RNA among African HIV-infected adults. Here, we report APOBEC3G genotypes and their influence on the disease progression rate in antiretroviral therapy (ART)-naïve Thai and Cambodian HIV-infected children with moderate immune deficiency.

Methods: ART-naïve HIV-infected children, aged 1-12 years old, CD4 15-24%, without severe HIV-related symptoms, were enrolled from 7 Thai and 2 Cambodian sites. The children were followed by physical examination; CD4%, CD4 counts every 12 weeks and HIV-RNA every 24 weeks until 144 weeks. ART were started when the CD4% was dropped to < 15% consecutively, or developed to the CDC category 'C events'. Genotyping of APOBEC3G genetic variants (186H/H, 186H/R or 186R/R) was performed to assess the genetic effect of APOBEC3G genotypes on rates of progression overtime; CD4%, CD4 counts, and plasma HIV-RNA.

Results: 147 children, 35% male, with a median (IQR) age of 6.5 (4.3-8.8) years were enrolled. 59% were Thai. The proportion of CDC clinical classification N:A:B were 1:63:36%. Median baseline CD4% was 20 (17-23)%, 605 (460-846) cells/mm3, and HIV-RNA was 4.7 (4.3-5.0) log10copies/mL. The frequencies of APOBEC3G genotypes AA (186H/H), AG (186H/R), GG (186R/R) were 86, 12, and 2%, respectively. Our random-effect linear regression analysis, after adjusted by baseline and study week, demonstrated that the APOBEC3G genotype GG was associated with significant decline in (95% confidence interval) CD4% -5.1% (-8.9 to -1.2%), p<0.001, and CD4 counts -226 (-415 to -34) cells/mm3, p<0.001. In contrast, the result showed no significant association between the APOBEC3G genotypes and changes of HIV-RNA log10 overtime (p=0.16).

Conclusions: Our data showed that a genetic variant of APOBEC3G genotypes, H186 in GG, was significantly associated with decline in CD4% CD4 counts over time in Thai and Cambodian ART-naïve HIV-infected children with moderate immune deficiency. Further studies should be evaluated for better understanding of APOBEC3G's antiviral effects on the disease progression in the HIV-infected children.

No conflict of interest
Abstract: P_12

HIV infection and adolescents

Characteristics of Perinatally HIV-Infected Adolescents in Asia: The TREAT Asia Pediatric HIV Observational Database

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Background: More perinatally HIV-infected children in Asia are reaching adolescence, and there are limited data on their long-term outcomes.

Methods: We analyzed data reported from 18 clinics in six countries participating in the TREAT Asia Pediatric HIV Observational Database (TApHOD). Data were longitudinally collected by centralized biannual data transfer. Available data from July 1991 to March 2011 were analyzed of children aged ≥12 years at their last evaluation (i.e., adolescents) who had at least six months of follow-up.

Results: Of 4,045 HIV-infected children in TApHOD, 1,254 (31%) were adolescents. Within a 3-year median follow-up time after age 12, 33 (2.6%) died, 52 (4.2%) were lost to follow-up, and 108 (8.6%) were referred to out. Of 1,061 adolescents on active follow-up, 485 (45.7%) were male and the current median (IQR) age was 14.7 (13.3-16.4) years, height for age z-score was -1.7 (-2.5 to -1.0), and body mass index was 18.0 (16.0-18.0) kg/m². At the most recent evaluation, 92.6% were receiving highly active anti-retroviral therapy (HAART; NNRTI+NRTIs = 70.6%), and 4% were receiving mono or dual NRTI, 71.2% (737 of 1035) had CD4 count >=500 cells/µL and 67.7% (718 of 830) had viral load <400 copies/mL. There were 770 (72.6%) adolescents had lost one or both parents, 93% attending school, and 62% with their HIV status disclosed to them. In multivariate analysis, having current WHO stage II (P= 0.04), currently being on a second-line regimen (P=0.006), and receiving no ART (P<0.001) were associated with recent VL >400 copies/mL. Current age >15 years (P<0.0001), CD4 <10% at ART initiation vs. 15-24% (P<0.0001), WHO stage II-IV (P <0.03), and duration of ART <1 year (P<0.02) were associated with recent CD4 <500 cells/mm³. Crude mortality was 0.93 per 100 person-years. Primary causes of death were opportunistic infections (45.4%) and other AIDS or treatment-related conditions (27.3%; e.g. lactic acidosis, renal failure, central nervous system conditions).

Conclusion: Initiating ART at earlier stage of HIV disease was associated with higher chance of immune recovery, and being able to maintain on first line regimen led to virologic control in adolescents. Perinatal HIV-infected adolescents were generally in good health status.

No conflict of interest
Abstract: P_13

HIV infection and adolescents

Darunavir/r once daily in treatment-naïve adolescents: 48-week results of the DIONE study

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Background: DIONE (TMC114-TiDP29-C230; NCT00915655) is a Phase II, 48-week, open-label trial of DRV/r 800/100mg qd plus zidovudine/lamivudine or abacavir/lamivudine in treatment-naïve, HIV-1-infected adolescents. The primary 24-week analysis showed DRV/r 800/100mg qd plus 2 NRTIs was effective and well tolerated in this population.

Methods: Patients aged 12 to <18 years, ≥40kg, viral load (VL) ≥1,000 copies/mL were eligible. For PK analysis, intensive sampling over 24 hours was performed after 2 weeks and sparse sampling after 4, 24 and 48 weeks of dosing. Safety, efficacy and resistance were assessed over 48 weeks.

Results: 12 patients (66.7% female; mean 14.6 years) were enrolled. Mean baseline VL was 4.72 log10 copies/mL, median CD4 cell count 282 cells/mm3 (median CD4% 18.3%). Six patients each received zidovudine/lamivudine or abacavir/lamivudine. At baseline, all patients were infected with virus susceptible to all commercially available PIs and NRTIs. After 48 weeks, 10/12 (83.3%) patients achieved VL <50 copies/mL (ITT-LOVR), 11/12 (91.7%) patients achieved VL <400 copies/mL; all had ≥1 log10 drop in VL versus baseline. Median CD4 increased by 221 cells/mm3 from baseline (ITT–NC=F). Most patients (83.3%) were always adherent for DRV/r intake. One patient was never-suppressed and one patient rebounded.

Conclusions: DRV/r 800/100mg qd plus 2 NRTIs was effective up to 48 weeks of treatment of HIV-1-infected, ARV-naïve adolescents, with comparable exposure to treatment-naïve adults. No new safety concerns were identified versus Week 24 or the DRV/r established safety profile.

Conflict of interest: financial relationship(s): CG, AN-J, SV and SW have no conflicts of interest to declare. PF has clinical trial agreements with Janssen and Bristol-Myers Squibb. SB has received support from Pfizer as an Expert, and support for his institution from Janssen for his participation in the DIONE trial. EL, TVdeC, PV and MO are full-time employees of Janssen.
Abstract: P_14

HIV infection and adolescents

Prevalence of Obesity and Lipid Abnormalities in a Cohort of HIV-Infected Pediatric and Adolescent Patients and Matched Controls

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Background: The relationship between HIV and obesity in pediatrics remains ill defined. The goal of this study was to describe the current state of obesity in a group of HIV-infected children and adolescents in New York City compared to matched uninfected controls.

Methods: 51 HIV-infected subjects and 51 age/gender matched controls, 3-20 years old, with a clinic visit between January 2009 and November 2011 were enrolled in this retrospective, cross-sectional study. Height, weight, BMI, total cholesterol, triglycerides, HDL, LDL, medical diagnoses and medications that might affect weight/lipid profiles were collected. HIV plasma RNA, CD4 count, and exposure to antiretroviral therapy (ART) were also collected in infected subjects. Classification as obese, overweight, normal weight or underweight was based on CDC standards. Univariate analysis was used to compare HIV status with BMI and lipid profiles.

Results: Weight and BMI z-scores were not significantly different in infected and uninfected groups (0.26 ± 1.4 vs. 0.55 ± 1.3, p=0.28; 0.61 ± 1.1 vs. 0.68 ± 1.2, p=0.77). There was a significant difference in height z-scores between groups (-0.59 ± 1.3 vs. -0.11 ± 0.96, p=0.03). There were no significant differences in rates of obesity between infected (18%) and uninfected groups (20%), p=0.10, or subgroups divided by gender and infection status, or between rates of being overweight in infected (27%) and uninfected groups (18%), p=0.15. There was a trend towards infected girls being more likely to be overweight than infected boys (39% vs. 13%, p=0.058). Rates of underweight or normal weight were similar in infected and uninfected subjects. In subjects with normal weight, total cholesterol, HDL and LDL values were similar in infected and uninfected subjects (157 ± 38 vs. 144 ± 22, p = 0.26; 47 ± 10 vs. 48 ± 9, p=0.78; 88 ± 30 vs. 83 ± 25, p=0.65), but triglycerides were significantly higher in infected vs. uninfected subjects (113 ± 70 vs. 53 ± 29 mg/dL, p=0.006). Triglyceride values in infected boys were strikingly higher than in uninfected boys (151 ± 75 vs. 47 ± 22, p=0.006). In obese subjects, total cholesterol, triglyceride, HDL and LDL values were not significantly different in infected compared to uninfected subjects (173 ± 29 mg/dL vs. 164 ± 18 mg/dL, p=0.48; 186 ± 101 vs. 126 ± 55, p=0.16; 42 ± 8 vs. 48 ± 8, p=0.17; and 95 ± 31 vs. 92 ± 22, p=0.83), nor were there significant differences in gender/ infection status subgroups. CD4 count, HIV plasma RNA, total time on ART and exposure to protease inhibitors was similar in the four weight categories.

Conclusions: Regardless of HIV infection status, many study subjects were either obese or overweight or had abnormal lipid values. While study subjects were similar in most comparisons, infected subjects were significantly shorter and had higher triglyceride levels than uninfected subjects. We also speculate that obesity masks the effects of ART on lipids since there were no significant differences in lipids based on infection status. Larger studies will be needed to define cofactors that explain these findings.

No conflict of interest

Abstract: P_15

HIV infection and adolescents

Follow up of a Cohort of HIV Positive Adolescents a Decade Later

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Introduction: Successfully transitioning youth with HIV into adult care is necessary as HIV/AIDS is now considered a chronic illness with long survival. We wanted to explore a decade later whether these youth who transition to adult care succeeded or fail with having regular medical care (at least 2 to 4 visits per year), are on antivirals medications and if they felt that they successfully transitioned into adulthood (finished school, GED, found jobs).

Methods: Charts were reviewed of all HIV+ youth enrolled in care prior to 1998 in an inner city HIV clinic. Youth still living and with contact information were consented to conduct a survey via telephone or direct interview.

Results: Of 35 youth identified: 17% had confirmed death; 23% had correct contact information (n=8) and agreed to be interviewed (3 females; 5 males). Of these 8: 88% were in care; 88% were introduced to adult clinical providers prior to transition; 75% were on Antiviral Medications; 75% had undetected viral loads; 100% reported that education and employment was regularly addressed by Adolescent clinic staff; 63% achieved educational goals (including completing a GED); 50% achieved employment goals; 50% experienced HIV stigma; 88% reported trusting relationship with adult providers, 75% had trusting relationships with adult providers; 100% had difficulty leaving the Adolescent Clinic for adult care. All 3 females reported getting pregnant and bearing children. None of the males had children.

Conclusions: Youth report difficulty leaving adolescent clinic for adult care. Youth providers can assist in successful transitioning to adult care by focusing on disease management as well assisting youth with education and employment goals. In addition, females will pursue childbearing.

Abstract: P_16

HIV infection and adolescents

A Practical Approach to HIV Disclosure to Children with HIV in Namibia

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Background: Disclosing HIV status to children has potential psychological benefits and positive implications for adherence but is recognized as a challenge worldwide. Katutura Hospital Paediatric ART Clinic in Windhoek, Namibia, serves about 460 children 6-18 years old. In November 2009, clinic staff began to use a booklet to explain to children how ARVs work. The booklet used simple language and cartoon sketches, describing HIV as a ‘bad guy’ who is kept sleeping by ARVs, thus allowing ‘soldiers’ (CD4 cells) to stay strong and keep the body healthy. This tool was used to assist in both partial and full HIV disclosure. Recording and monitoring tools were developed and implemented. This study examines baseline information about the children enrolled in the first 5 months of the disclosure program and analyses changes in how children understood why they take their medicine in a subset who had at least one repeat visit during the study period.

Materials and Methods: Records of all children ≥6 years old enrolled in the HIV disclosure program and introduced to the booklet between November 2009 and April 2010 were reviewed. Baseline data were extracted on age at enrolment, gender and years on HAART. The child’s answer to the question ‘Why do you take your medicines?’ as recorded in the monitoring tool on enrolment was extracted and for those with a repeat visit, it was compared with the answer given at the follow-up visit.

No conflict of interest
**Results:** During the study period, 301 children aged 6-19 (>60%) were enrolled in the program and introduced to the booklet during routine clinic appointments. Mean age was 10.8 years, 49% females. Of 297 on HAART, the mean time on HAART was 3.7 years. Of children ≥10 years, 66% knew their HIV status, compared to 8% of those <10 years. Of children who did not know their HIV status, most stated they 'did not know' why they took their medicine and some mentioned other illnesses, such as TB, or simply that they are sick. Being on HAART >1 year was associated with greater chance of knowing HIV status. Follow-up data was available for 61 children. At baseline, 47% of these said they 'did not know' why they take their medicine compared with only 2% at follow-up. The majority were able to describe their partial understanding of the disease based on the booklet or full understanding of their disease.

**Conclusions:** Introduction of a practical partial and full HIV disclosure tool to a busy paediatric clinic is possible. These initial results informed a decision to adapt the materials and roll them out to all HIV clinics throughout the country.

**No conflict of interest**

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**Abstract: P_17**

**HIV infection and adolescents**

**Quality of life in HIV-infected children using treatment simplification to lopinavir/ritonavir monotherapy**

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**Background:** There are limited data of quality of life (QOL) in HIV-infected children after treatment simplification. We reported QOL in HIV-infected children after switching to lopinavir/ritonavir monotherapy (mLPV/r).

**Methods:** HIV-infected children with HIV-RNA <50 copies/ml while using second-line double boosted protease inhibitors (dPI) were switched to mLPV/r. Primary caregivers completed age group-specific Pediatric AIDS Clinical Trials Group (PACTG) QOL questionnaires at week 0, 24, and 48. The questionnaires assessed 6 QOL domains: general health rating, physical functioning, psychosocial well-being, social and role functioning, health care utilization, and symptoms. The raw scores from each domain were transformed to a 0 to 100 scale with the following formula: Transformed score = [(actual raw score – lowest possible raw score)/ (highest possible raw score – lowest possible raw score)] x 100. Higher transformed scores indicate better health in that domain.

**Results:** 40 Thai HIV-infected children were enrolled. Median (IQR) age was 11.7 (10.2-13.5) years, 50% were female, %CDC N:A:B:C was 22:55:18:5%. At enrolment, 36 (90%) children used LPV/r+ saquinavir, 4 (10%) used LPV/r+ indinavir and 11 (27.5%) children used lamivudine as well. Median CD4% was 27 (23.5-29.5%). 60% of children knew their HIV status. 47.5% of primary-caregivers were biological parents. At weeks 48, none died or lost to follow up. When compared mean (SD) QOL scores between weeks 0 vs. 48, no significant changes of QOL scores were found in all domains;

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**Conclusion:** When using a multidimensional assessment of general QOL, our study failed to detect significant changes of QOL after simplification to lopinavir/ritonavir monotherapy.

**No conflict of interest**
Abstract: P_18

HIV infection and adolescents

Risk Behaviors and Treatment Adherence among HIV-infected Adolescents in the TREAT Asia Pediatric HIV Observational Database

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Background: With scale-up of antiretroviral therapy (ART), increasing numbers of HIV-infected children have been surviving into adolescence. However, the challenges of negotiating the transition from adolescence to adulthood are complex in this group living with a stigmatized, chronic disease. As a consequence, HIV-infected adolescents may face problems with ART adherence, exhibit risk-taking behaviors, and be vulnerable to abuse or violence. This study sought to collect information on adherence and behavioral risk factors in HIV-infected adolescents who are being followed in TREAT Asia Pediatric HIV Observational Database (TApHOD) sites to inform decisions related to long-term management.

Material & Methods: Fifty HIV-infected adolescents aged 10-18 years who were disclosed to about their HIV status were enrolled from 5 TApHOD network sites TApHOD in Malaysia and Thailand. Participants were asked to complete a questionnaire at baseline and week 24 using an audio computer-assisted self-interview (ACASI). A maximum total of 103 questions were included, collecting information on general and social demographics, sexual behavior, substance abuse, adherence to ART, stigma, and violence.

Results: Forty-six adolescents completed the questionnaire; 26 (57%) were Malay and 25 (54%) were female. Median (IQR) age was 14 (12-16) years. Twenty-eight (61%) were studying in secondary school or above, and the majority (63%) lived with their parent(s). Median (IQR) duration on ART was 5 (4-7) years, and 35% reported current difficulties taking ART; 72% had self-reported adherence more than 95%. Eleven (24%) reported that they had tried alcohol at a median (IQR) age of 15 (13-15) years, 5 (11%) had tried cigarette smoking at a median (IQR) age of 13 (13-15) years old, and 1 reported ever using marijuana. One male and 4 females (11%) had engaged in sexual intercourse, with age at sexual debut between 14 and 16 years; 4 (9%) reported having unprotected sex after using alcohol or illicit drugs. Level of adherence was not significantly associated with reporting risk-taking behavior. Two adolescents reported problems going to school because of their HIV infection, and 24% had a negative body image. Experience with physical abuse was reported by 7 (15%) adolescents by family members, 9 (20%) by friends, and 3 (6.5%) by teachers; 1 reported having been sexually abused. At week 24 of the study, 18 (39%) adolescents repeated the ACASI; all were Thai and 10 (56%) were female. There were no significant differences between week 0 and 24 in the levels of self-reported adherence, use of alcohol, cigarette smoking, or physical abuse (p >0.05).

Conclusions: Although, the percentages of Asian HIV-infected adolescents in this pilot study reporting risk-taking behaviors, adherence problems, or having experienced stigmatization and violence were generally low, appropriate psychosocial interventions are needed to prevent and address these issues in HIV-infected adolescents aging into adulthood.

No conflict of interest
Abstract: P_19

Complications of HIV therapy

High HbA2 due to zidovudine exposure: implication for β-thalassemia trait screening


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Background: High hemoglobin A2 percentage (HbA2>3.5%) has been used as a screening test for β-thalassemia trait. However, high %HbA2 can occur in HIV infection or after zidovudine(ZDV) exposure. This study was performed to compare the %HbA2 in HIV-infected children in antiretroviral (ARV) naive and ZDV-exposed groups to explore the appropriate method to interpret the Hb typing result in these children.

Methods: This is a sub-study of the PREDICT study, a randomized controlled trial of immediate vs. deferred ARV initiation in ARV-naive HIV-infected Thai and Cambodian children. The hemoglobin typing and red blood cell indices at 12 weeks after enrollment were collected in both groups. ZDV exposure at least 8 weeks is needed to be enrolled in ZDV-exposed group. Children with HbE trait and disease were excluded. DNA analysis for common mutations in β-hemoglobin genes were performed in all enrolled children.

Results: 222 HIV-infected children were enrolled. 111 were in the ZDV-exposed group. Baseline clinical and laboratory characteristics were shown in Table 1. Abnormal %HbA2 was found in 59.5% of ZDV-exposed compared to 6.3% of ARV-naive children (p <0.001). Two β-thalassemia trait children were found in the ZDV-exposed group with the %HbA2 of 6.4 and 6.6 respectively. Using low MCH and/or MCV reduced the abnormal HbA2 interpretation from 59.5% to 4.5% and from 6.3% to 1.8% in ZDV-exposed and ARV-naive groups respectively. Using these 3 abnormal parameters, only 2/7(28.6%) were β-thalassemia trait from DNA analysis.

Conclusions: Abnormal high %HbA2 were found in more than a half of ZDV-exposed HIV-infected children. Using the standard HbA2>3.5% cut-off level for β-thalassemic trait could lead to misdiagnosis. Using low MCV and MCH were important co-parameters to reduce the misinterpretation of β-thalassemia trait. However, the DNA analysis should be performed to confirm the diagnosis in this situation.

No conflict of interest

Abstract: P-20

Complications of HIV therapy

Dermatologic immune reconstitution inflammatory syndrome (IRIS) in children receiving HIV treatment from a community outreach program

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Introduction: Little information exists on how antiretroviral therapy (ART) affects the course of dermatologic conditions in children whereas in adults dermatological manifestations of Immune reconstitution inflammatory syndrome(IRIS)
appear to be the most frequent. A study (Orikiiriza, 2011) demonstrated that dermatological manifestations were the most common IRIS events in children receiving ART. Caregivers get concerned with florid manifestations of popular pruritic eruptions (PPE) in children receiving ART and there is extensive use of betamethasone cream and local herbs to help alleviate symptoms. The aim of this study was to find the incidence of dermatological-IRIS in children receiving ART for at least 12 weeks.

**Methods:** Medical charts of 110 children who received ART from a community outreach program in Namuwongo, Kampala between January 2010 and September 2011 were reviewed retrospectively. Data on skin conditions and treatment recorded by medical officer on visit after children start ART was entered into MExcel. The child’s immunological status prior to ART initiation and at 3 months after ART usage plus demographic data were collected. Exclusion criteria: charts of children whose skin conditions necessitated change in ART regimen before the symptoms resolved; and children with recorded non-continuous adherence to ART. Data was exported to and analysed using STATA program.

**Results:** A total of 110 charts reviewed gave median age 6.1 years (IQR 9months-12years). Females were 70 (63.6%). All patients received trimethoprim-sulfamethoxazole at ART initiation. Baseline characteristics; children with CD4+% <15% were 77(70%), >= 15% were 33children. Viral load >399,000 copies were 76 children (69.1%) and <=399,000 were 34children. There were 85children (77.2%) in WHO stage III/IV at baseline. Median time on ART was 24weeks (IQR 13.2-40.8). PPE had the highest incidence (47cases) after ART initiation. 10cases of verrucae planae, 9 cases of Kaposis Sarcoma, Herpes Zoster and Tinea corporis each, 8molluscum contagiosum, 4tinea capitis, 3HSV and 1case of varicella zoster. Median time to develop PPE was 3weeks (IQR 13.2-50.9days). Increasing age was associated with IRIS; highest in children aged between 5-12 years (age correlated with degree of immunosuppression).

**Conclusion:** The prevalence of unmasking dermatological-IRIS was high for in these children. PPE accounted for highest mucocutaneous IRIS manifestations. Caregivers should be counselled about possible worsening of PPE with ART initiation.

No conflict of interest

**Abstract: P_21**

**Complications of HIV therapy**

**Bone fractures among HIV-infected and HIV-exposed, uninfected (HEU) children in Latin America**

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**Introduction:** HIV and its treatment may be associated with low bone density in some children, but the clinical consequence of this is unknown. We compared bone fracture incidence rates between HIV-infected and HIV-exposed, uninfected (HEU) children in Latin America.

**Materials & Methods:** Retrospective fracture data were collected on HIV-infected and HEU children participating in the NISDI (NICHD International Site Development Initiative) multicenter, prospective cohort study at clinical sites in Brazil, Argentina, Mexico, and Peru.
Fracture history was obtained by parent/caregiver interview using a structured questionnaire. Rates and features of first fractures were summarized and compared for HIV-infected and HEU children.

**Results:** Information on bone fracture history was obtained from 96% (480 of 500) HIV-infected children and 89% (444 of 498) HEU children. Among the HIV-infected children, 4.4% (21 of 480) reported at least one fracture as compared to 1.8% (8 of 444) of HEU children. The number of children who experienced more than one fracture was similar in the two groups (p-value = 1.0). At interview, HIV-infected children were older than HEU children (mean age 7.4 vs. 2.4 years, p-value <.0001). Most fractures (57.1% in HIV-infected and 50% in HEU) resulted from slight trauma, defined as falling to the ground from standing on the same level or falling <1.5 feet as opposed to moderate or severe trauma (p-value=0.34). The overall distribution of fractures by body part was similar in the two groups (p-value =0.51), although upper extremity fractures accounted for 71.4% (15 of 21) of fractures in HIV-infected children versus 50.0% (4 of 8) of fractures in HEU children. HIV-infected children were older than HEU children at first fracture (mean age 5.4 vs. 1.9 years, p-value <.001). Limited to the first 5 years of life, the fracture incidence rate (IR) was 4.4 per 1000 person-years among HIV-infected children and 6.2 per 1000 person-years among HEU children. The IR ratio was 0.71 (95% CI 0.28, 1.80). Additional antiretroviral drug (ARV) use and clinical data are available on children (11 HIV-infected and 7 HEU) whose fractures occurred while enrolled in NISDI (62% of all children with fractures). All 7 HEU children had used zidovudine prophylaxis during the neonatal period but not other ARVs. Among the 11 HIV-infected children, all had used nuclease reverse transcriptase inhibitors, 64% (7) had used nonnuclease reverse transcriptase inhibitors (NNRTIs), 64% (7) had used protease inhibitors (PIs), and 36% (4) had used both PIs and NNRTIs before the time of fracture. One HIV-infected child (9%) had used tenofovir and three (17%) had used stavudine. The proportion of children with normal height and weight z-scores at the time of fracture was similar in the two groups.

**Conclusions:** The risk of fracture was similar in these cohorts of HIV-infected and HEU children. Longer term and larger studies will be necessary to address whether HIV-infected children are at increased risk of fractures.

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Abstract: P_22

**Complications of HIV therapy**

**Mitochondrial Function & Metabolic Abnormalities in Children with Perinatally-Aquired HIV Infection in the Pediatric HIV/AIDS Cohort Study (PHACS)**


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**Introduction:** Metabolic abnormalities, common among perinatally HIV-infected children (HIV+), may be caused by mitochondrial dysfunction that is induced by antiretroviral therapy (ART) or chronic viral infection. We compared mitochondrial function [oxidative phosphorylation (OXPHOS) enzyme activities and lactate levels] of HIV+ and HIV-exposed, uninfected (HEU) children. Among HIV+ children, associations with fasting glucose, insulin, and homeostatic model assessment of insulin-resistance (HOMA-IR) were determined.

**Material and Methods:** HIV+ and HEU were enrolled from the PHACS Adolescent Master Protocol. Children with known, non-HIV- associated mitochondrial disorders were excluded. Demographic and BMI [all children] and CD4, HIV viral load, ARV exposures, and fasting insulin/glucose [HIV+ only] were collected. Main outcomes included venous and point-of-care (POC) lactate, venous pyruvate, and peripheral blood mononuclear cells (PBMC) NADH dehydrogenase (CI) and cytochrome c oxidase (CIV) enzyme activities. A Fisher's
Exact Test and Wilcoxon test were used to compare outcomes between HIV+ and HEU; Spearman correlations were determined between insulin/glucose and OXPHOS activity in HIV+.

**Results:** 112 HIV+ and 66 HEU children were enrolled as of December 2011. HIV+ children were older than HEU (15.8yrs vs 12.4yrs) with similar gender and racial distributions. BMI-Z score was lower in HIV+ children (0.41SD vs 0.54SD). Among HIV+ children, 45% were CDC stage B/C and 74% had CD4 >500 cell/mm³ with 60% having viral load <400cp/mL. Fifty-six percent were on HAART, PI-based ARVs. Median glucose was 87mg/dL (range 74-110), insulin was 13.6 IU (range 4.7-83) and HOMA-IR was 3.1 (range 1-20.7). POC lactate was higher (1.6 mmol/L [IQR 1.2, 1.9] vs 1.3 mmol/L [IQR 1.0, 1.8]; P=0.06) and venous pyruvate lower (1.0 mmol/L [IQR 0.79, 1.43] vs 1.4 mmol/L [IQR 1.0, 1.87]; P=0.001) among HIV+ vs HEU children, respectively. OXPHOS CI activity was 17.6 OD/min/ug e⁻⁶ [IQR 11.0, 26.7] in HIV+ children vs 18.2 OD/min/ug e⁻⁶ [IQR 13.5, 26.6] in HEU children; (P=0.35) and CIV was 23.7 OD/min/ug e⁻⁶ [IQR 19.2, 29.1] in HEU children; P=0.75), OXPHOS activities did not differ between HIV+ vs HEU respectively. Among HIV+ with measures available, we observed a negative correlation of fasting glucose with CI OXPHOS activity (n=26; r=-0.38; p=0.06) and a positive correlation with venous lactate (n=34; r=0.31; p=0.07).

**Conclusion:** Preliminary analyses show higher POC lactate in HIV+ compared to HEU children and that mitochondrial dysfunction may be associated with metabolic abnormalities in HIV+ children.

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**Abstract: P_23**

**Complications of HIV therapy**

**A Provider Survey of Initiation of Antiretroviral Therapy in Youth with HIV**

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**Background:** In December 2010, the Department of Health and Human Services (DHHS) guidelines for initiation of antiretroviral therapy (ART) for adolescents and adults with HIV changed to recommend initiation of ART with CD4 counts ≤ 500 (rather than ≤ 350). Little is known about the knowledge, attitude, and practice barriers experienced by providers in the United States regarding ART initiation in adolescents and this recent recommendation.

**Methods:** We administered an anonymous web-based survey to providers in the HIV Medicine Association network caring for behaviorally infected youth with HIV, age 13-25 years. The 21 item survey assessed potential knowledge, attitude, and practice barriers associated with initiation of ART using clinical vignettes and questions with forced choice format and Likert scales.

**Results:** Thus far, 290 of 2211 (13%) potential respondents completed the survey (59% female; 65% physicians, 24% nurse practitioners, 9% physician assistants, 2% other). Respondents had a mean of 13 years (range of 1-30 years) experience treating youth with HIV. The distribution of respondents' zip codes who responded to the survey corresponded to areas of high HIV prevalence in the United States. When presented with a clinical vignette describing an adolescent presenting with a CD4 count in the 350-500 cells/mm³ range, the majority (96%) reported they would initiate ART. However, only half (54%) correctly identified that this is the current DHHS recommendation. When presented the same clinical vignette in an adolescent presenting 5 years ago, only 23% would have initiated ART. Respondents identified more patient-specific barriers than...
practice barriers when considering initiation of ART (Table 1).

**Conclusions:** Respondents agreed with the current DHHS recommendations to initiate ART in youth with HIV with CD4 counts < 500 cells/mm³. Patient barriers were more commonly identified than practice barriers. Strategies directed to reduce these barriers could facilitate earlier initiation of ART in younger patients with HIV.

**Table 1: Barriers to ART Initiation In Youth with HIV**

<table>
<thead>
<tr>
<th>Barrier</th>
<th>Large barrier (%)</th>
<th>Small barrier (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unstable housing</td>
<td>55</td>
<td>45</td>
</tr>
<tr>
<td>Not disclosed to family/friends/partners</td>
<td>31</td>
<td>69</td>
</tr>
<tr>
<td>Concerning use of recreational drugs</td>
<td>66</td>
<td>34</td>
</tr>
<tr>
<td>Lifestyle not conducive to daily medications</td>
<td>88</td>
<td>12</td>
</tr>
<tr>
<td>Provider lacks time/ancillary staff to counsel patient</td>
<td>17</td>
<td>83</td>
</tr>
</tbody>
</table>

**Materials and Methods:** This was an exploratory study undertaken at Delhi, India. Pupose sampling was used to select the participants from the nongovernmental organizations working for families living with HIV/AIDS. Participants included thirty children who were in the age group of 07-14 years (mean age 11.17 years) and their primary caregivers mainly the mothers. We used face to face interviews with children and their primary care givers, observations, standardized test ‘Self Perception Profile’ developed by Susan and Harter and narratives of children as tools of data collection. Qualitative analysis of children’s responses was done. Student test was used to ascertain significant difference in the behavioural conduct of children on the basis of HIV status, gender, age and orphanhood. Most children had more than one behavioural issue.

**Results:** All children reported experiences of violence either due to their own or their parent(s) HIV status and more than 80% of the children had behavioural issues. Deprivations associated with progressive HIV infection aggravated the behavioural issues in children living with HIV/AIDS. Aggression (27) was the most frequently reported behavioural issue. Besides this, other behavioural problems like truancy (3), mood swings (21), stubbornness (24), use of abusive language (18), disobedience (21), sleep disturbances (9), bruxism (2), nightmares (7), pica (1), fear of ghosts (3), bed wetting (5), speech disorders (2) were also reported. Most children had more than one behavioural issue. Twelve children scored below the mean on behavioural conduct—a subdomain of Self Perception Profile. The p values were not significant for HIV status, gender, age and orphanhood.

**Conclusions:** Our data raise concern regarding the impact of societal attitudes towards the children living with HIV/AIDS and violence against them which puts them at a risk of developing behavioural issues. Provisions of free regular mental health checkups and optimal care and support services for children living with HIV/AIDS are essential for their all-round development besides awareness generation strategies about HIV/AIDS for general public at a war scale. Provision of free services is a critical incentive to avail care. Innovative and feasible measures are urgently required in this direction.

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**Abstract: P_24**

**Comprehensive Pediatric HIV care**

**Violence against children living with HIV/AIDS and emergence of behavioural issues in children**

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**Background:** The children living with HIV/AIDS are at increased risk of facing violence against them. A few studies have examined the co-occurrence of violence against children with HIV/AIDS, deprivations caused by progressive HIV infection and emergence of behavioural issues in them. The objectives of the study were to investigate the impact of violence against children with HIV/AIDS, deprivations caused by progressive HIV infection in families and emergence of behavioural issues in them.

**Results:** All children reported experiences of violence either due to their own or their parent(s) HIV status and more than 80% of the children had behavioural issues. Deprivations associated with progressive HIV infection aggravated the behavioural issues in children living with HIV/AIDS. Aggression (27) was the most frequently reported behavioural issue. Besides this, other behavioural problems like truancy (3), mood swings (21), stubbornness (24), use of abusive language (18), disobedience (21), sleep disturbances (9), bruxism (2), nightmares (7), pica (1), fear of ghosts (3), bed wetting (5), speech disorders (2) were also reported. Most children had more than one behavioural issue. Twelve children scored below the mean on behavioural conduct—a subdomain of Self Perception Profile. The p values were not significant for HIV status, gender, age and orphanhood.

**Conclusions:** Our data raise concern regarding the impact of societal attitudes towards the children living with HIV/AIDS and violence against them which puts them at a risk of developing behavioural issues. Provisions of free regular mental health checkups and optimal care and support services for children living with HIV/AIDS are essential for their all-round development besides awareness generation strategies about HIV/AIDS for general public at a war scale. Provision of free services is a critical incentive to avail care. Innovative and feasible measures are urgently required in this direction.

*No conflict of interest*
Abstract: P_25

Comprehensive Pediatric HIV care

Using quality improvement methodologies to improve quality of pediatric HIV care and initiation of ART – Tanzania

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Introduction: Supporting the Ministry of Health and Social Welfare’s (MOHSW) National HIV program in five regions of Tanzania, the Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) introduced quality Improvement (QI) initiatives to assess and improve quality of care provision. In 2010, using a structured QI approach EGPAF attempted to improve antiretroviral therapy (ART) uptake and retention among children.

Methods: Ten public health facilities, where less than 70% of enrolled HIV infected infants had started ART, were selected for improvement activities (Global AIDS System for Evaluation & Reporting, Jan-March 2011). Medical records of children aged 0 to 14 years were randomly selected to assess quality using internationally recognized HIV quality care indicators. Baseline assessment of 339 pediatric files from January to June 2011 revealed: 75% of eligible children started ART, 73% had clinical staging reflecting nutrition status, 68% had baseline CD4 test, 78% had a clinical review and 63% had adherence assessment in the last six months. Low rates of CD4 testing and incorrect WHO-staging resulted in some eligible children not starting ART. To improve, EGPAF and MOHSW staff provided on-site mentoring on WHO-staging using growth monitoring tools. Notes on files reminded clinicians to conduct CD4 testing, staff improved adherence counseling and traced defaulters.

Results: A repeat assessment of 431 pediatric files from July to December 2011 suggested an overall statistically significant difference between baseline and repeat score at (z = -2.812, and p = 0.0049); 89% of eligible children started ART (z= -2.497, p=0.0125), 87% had clinical staging reflecting nutrition status (z= -2.395, p=0.0166), 77% had CD4 test at enrollment (z= -2.092, p=0.0364), 86% of children had clinical review in the last 6 months (z= -1.533, p=0.1253) and 81% had a documented adherence assessment (z= 2.601, p=0.0093).

Conclusion: QI methods enabled staff to identify and focus efforts to improve WHO staging, CD4 testing, and adherence resulting in improved ART initiation, and retention in care.

No conflict of interest

Abstract: P_26

Comprehensive Pediatric HIV care

Cognitive, neurological and adaptive behaviour functioning among children with perinatally-acquired HIV infection in India

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Introduction: With improved survival of HIV-infected children, neurocognition is an important area to address. The aim of this study was to examine the effects of HIV infection on cognitive, neurological, and behavioral functioning on children by comparing these areas in perinatally-acquired HIV-infected and HIV-uninfected children.

Materials and methods: HIV-infected children (4-15yrs) were recruited from a tertiary-care center in India, along with HIV-negative children matched for age, gender and income status. Perinatal infection was confirmed by history and/or documentation of the child’s mother being...
HIV-infected, and absence of other risk factors of HIV infection acquisition in the child. Those with HIV encephalopathy were excluded. Among those who were HIV-uninfected, excluded children were those with a known chronic illness, and no history of congenital or acquired cognitive impairment. Assessment tools included (i) soft neurological signs: Physical and Neurological Examination for Soft Signs (PANESS); (ii) neurocognition: culturally-adapted Wechsler Preschool and Primary Scales of Intelligence (WPPSI), Wechsler Intelligence Scale for Children (WISC-III); (iii) adaptive behaviour: Vineland Adaptive Behaviour Scales (VABS). Statistical analysis was performed using descriptive statistics, chi square tests, univariate and multivariate regression analyses.

Results: We studied 167 children, (82 HIV-infected, 85 HIV-uninfected) with 56% males and mean age 8.6yrs. Total IQ scores were lower among HIV-infected children compared to HIV-uninfected children (74.9 ±12.9 versus 87.9 ±15.4, p< 0.001). Both domains of verbal IQ and performance IQ were uniformly affected. Severely immunosuppressed children (CD4 <20%) had lower total IQ scores (70.7 ±12.3) compared to those with CD4>20%, (IQ 77.1 ±12.8, p=0.03). Viral load and ART status has no effect on IQ scores. Multivariate regression revealed that HIV status, weight-for-age Z-score and hemoglobin were independent factors that affected IQ scores (adjusted r²=0.25, p=0.006). The presence of HIV infection independently decreased IQ scores by 9.22 units. PANESS scores were higher among HIV-infected children compared to uninfected children (HIV-positive mean score: 7.5, [3, 13.3]; HIV-negative mean score: 4.0, [1.5, 9.5], p=0.02) suggesting higher degree of subtle neurological abnormalities among HIV-infected children. Adaptive behaviour scores were similar for both HIV-infected and uninfected children irrespective of age and sex. Among HIV-infected children, adaptive behavior performance was decreased among those who were immunosuppressed (VABS score 91.2 vs 96.1 among those with CD4<20% and > 20% respectively, p = 0.02). The presence of ART among HIV-infected children did not affect adaptive behaviour scores.

Conclusions: HIV-infected children had lower IQ scores and higher prevalence of soft neurological signs compared to HIV-uninfected children, indicating that subtle neurocognitive impairment is an important feature of perinatally-acquired HIV infection, particularly among those with poor nutritional status. We recommend routine neurocognitive assessment and suggest that early intervention with initiation of ART before the onset of severe immunosuppression may improve neurological outcomes in these children.

No conflict of interest

Abstract: P_27

Comprehensive Pediatric HIV care

Feasibility and challenges of Isoniazid Preventive Therapy and Intensive Case Finding in the paediatric HIV care package of a low-income setting

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Introduction: In January 2011 intensified tuberculosis case-finding (ICF) and isoniazid-preventive-therapy (IPT) were included by WHO in the paediatric HIV care package and a new clinical algorithm was set up to rule out active tuberculosis (TB) in low-income settings. The endorsement of this new recommendation has been slow, and the implementation is facing considerable challenges.

Material and Methods: In January 2011 ICF/IPT were started at Nsambya Home Care (NHC) of S. Raphael of S. Francis Nsambya Hospital (Kampala-Uganda), according to WHO guidelines. Children attending the HIV clinic were evaluated with a 3 steps collection of information such as: 1) TB contact history, past TB episodes, BCG vaccination; 2) clinical signs (current cough, fever, failure to thrive); 3) IPT initiation and lab monitoring (clinical follow-up, adherence). Children without TB started 6
months of IPT and were routinely evaluated. Liver function tests (LFTs) were performed at initiation and week 4 in order to assess drug safety. Statistical analysis was conducted with SAS and chi-square, fisher exact test, t-test and logistic regression were performed. An operational survey was conducted to assess the health care workers (HCW) opinion one year after the ICF/IPT implementation.

Results: From Jan 2011 to Jan 2012, 360 (M 175, F 185) out of 987 children enrolled in the program were screened. 159 (44%) children (76% on ARVs) started IPT within a median time of 112 days (IQR 64-184). Only 3 (1.9%) stopped IPT because of liver toxicity (n=2) or poor adherence (n=1). The absence of clinical signs (p=0.007) or failure-to-thrive (p=0.04) at enrolment were related with IPT initiation within 30 days of enrolment, while IPT initiation within 30 and 60 days was associated with female sex (p=0.048 and p=0.01, respectively) and a recent LFTs assessment (p=0.02 and p=0.01). Adherence (>90% visits/year) to monthly follow-up (106 out of 159 children compared to 74/201; p<0.0001) and high CD4 z-score at enrolment (mean/SD +1,44/12 compared to -1,25/10; p=0.03) were associated with IPT initiation, not with an earlier initiation, both at univariate and multivariate analysis. One year after the ICF/IPT implementation all the HCW agree that the clinical WHO algorithm is useful but only 15% think that IPT is easy to be implemented. Three main reasons were associated to the delay in starting IPT: poor ARVs adherence, the absence/impaired LFTs at enrolment and the overall pills burden.

Conclusions: Our experience shows that the inclusion of WHO 2011 ICF/IPT algorithm within the HIV care package is feasible and instrumental to enhance TB diagnosis. We confirmed IPT to be safe and tolerable even outside clinical trial settings. However, operational challenges lead to significant delays in IPT initiation, likely to be due to the low specificity of the screening algorithm and the social factors affecting retention in care and adherence.

No conflict of interest

Abstract: P_28
Comprehensive Pediatric HIV care

Nutritional characteristics of HIV-infected pregnant women and their infants – an NICHD NISDI LILAC sub-study

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Background: The nutritional status of HIV-infected pregnant women and their infants in Latin America has not been well studied. Our objectives were to: 1) assess micronutrient plasma concentrations among pregnant, HIV-infected women and their infants; and 2) evaluate changes in infant micronutrient status from birth to 6 months (6M).

Methods: Our sub-study included three sites from the NISDI LILAC prospective cohort study of HIV-infected pregnant women and their children in Latin America. Weight, height, and blood concentrations of retinol, plasma α-tocopherol, ferritin, and zinc were obtained from mothers after delivery and infants at birth and 6M. Retinol and α-tocopherol were quantified by high performance liquid chromatography and zinc by atomic absorption spectrophotometry. Deficiency were defined as: zinc (mg/dL) <64 (infants) and <50 (mothers); retinol (mmol/L) <0.7; α-tocopherol (mmol/L) <12 (infants) and <7 (mothers); ferritin (ng/mL) <10 (mothers), <25 (infants aged ≤1M), <50 (infants 2M to < 6M), and <7 (6M to 15 years). Maternal gestational age-adjusted BMI <19.8 was considered underweight.

Results: Of 97 participating women, 19.6% were underweight. Women were most often zinc deficient (41%), with lower rates found for other micronutrient deficiencies (retinol: 12.5%; α-
tocopherol: 1.0%; ferritin: 16.3%). Infant deficiency rates decreased from birth to 6M for each micronutrient (zinc: 36.8% to 17.5%; α-tocopherol: 81.1% to 18.5%; and ferritin: 55.3% to 27.4%). The ORs for micronutrient deficiency among underweight women (versus normal weight women) were 1.5 (95% CI: 0.5-4.3), 0.6 (95% CI: 0.1-3.3), and 1.6 (95% CI: 0.4 -6.1) for zinc, retinol, and ferritin, respectively. The ORs for micronutrient deficiency at birth among infants born to underweight women were 0.9 (95% CI: 0.3-2.7), 0.5 (95% CI: 0.1-1.9), 0.5 (95% CI: 0.1 -1.7), and 2.0 (95% CI: 0.6 -6.1) for zinc, retinol, α-tocopherol, and ferritin, respectively (p>0.05).

Conclusions: Micronutrient deficiencies were common among women and their infants. Prevalence of infant deficiencies was lower at 6M for all micronutrients. Underweight women and their infants, at birth, were not at increased risk for micronutrient deficiency.

No conflict of interest

Abstract: P_29

Comprehensive Pediatric HIV care

Early pediatric access to HIV care of HIV-exposed children in Ouagadougou, Burkina Faso: situational analysis in 2010.


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Background: World Health Organization recommended a universal antiretroviral therapy for all Human Immunodeficiency Virus (HIV)-infected children before 2 years of life in 2010 but this roll-out imposes to identify early enough these children. We described the access to pediatric HIV diagnosis and care in Ouagadougou, the capital of Burkina Faso, in 2010, before the implementation of an international randomized clinical trial to assess simplified strategies for triple antiretroviral therapy in HIV-infected children initiated on treatment before two years of age in Africa.

Methods: A cross-sectional survey was undertaken in 2010 in all health facilities delivering paediatric HIV services in Ouagadougou, before the implementation of MONOD trial. A desk review was carried out and semi-structured questionnaire was administered to the personnel to assess the health centres according to the World Health Organisation standards.

Results: In 2010, there was no treatment and care at primary health care level for HIV-infected children in Ouagadougou; five district hospitals, one confessional hospital and two University Hospital Pediatric Departments provided paediatric HIV care. Among the 77,855 expected pregnancies in 2009 in these services, 56,715 attended at least one antenatal consultation (72.8%). Among them, 50,489 had access to counseling & testing HIV services (89.0%), and 45 376 accepted to be tested (89.9%). The HIV-prevalence was 2.35% (95% CI: 2.2%-2.5%) and 441 (41.4%) pregnant women benefitted from Prevention of Mother-to-Child Transmission intervention, using a protocol based on zidovudine, lamivudine and nevirapine. Furthermore, 784 HIV-exposed infants (0-2years) were tested post-natally (73.5%) and 147 were found to be HIV-infected, 18.8% (95% CI: 16.0%-21.5%). In 2010, a total of 28 children <2 years were initiated an antiretroviral therapy in these sites (19.0%), and Stavudine - Lamivudine- Nevirapine was the most prescribed first-line regimen (77.7%). Pediatric HIV services are hindered by operational challenges: shortage of infrastructures and qualified health care staff, shortage of antiretroviral drugs supply and pediatric formulations, lack of maintenance of medical devices, lack of transportation system to organize the HIV-testing management.
Conclusion: Despite an overall good access to prenatal and postnatal HIV testing services in Ouagadougou in 2010, there are still many missed opportunities for both the prevention of mother-to-child transmission and the access to early HIV infant diagnosis. The national HIV care program should make a commitment to include urgently a better management of human and material health resources to promote a universal and early access to pediatric HIV care services in Burkina Faso.

No conflict of interest

Abstract: P_30

Comprehensive Pediatric HIV care

Trends in Provider Initiated Counseling and Testing and Enrollment into Care of children at ICAP supported Health Facilities in Ethiopia


Background: HIV-infected children contribute to 14% of the HIV/AIDS deaths worldwide, however they account for only 6.9% of the total on ART. HIV testing is the first critical entry point to a continuum of HIV healthcare. In 2007, WHO and UNAIDS recommended that in countries with HIV prevalence consistently over 1% in pregnant women, all persons attending health facilities should be offered provider initiated HIV testing and counseling (PITC). We describe trends in pediatric HIV testing and enrollment at ICAP-supported facilities in Ethiopia.

Materials and Methods: ICAP in Ethiopia supports comprehensive HIV/AIDS care and treatment (C&T) in 69 health facilities in four regions; Oromiya, Somali, Dire Dawa and Harari. In 2007, PITC was implemented at the following service delivery points; adult and pediatric inpatient care units and outpatient departments (OPDs). All clients accessing services at these points were offered HIV testing as part of routine care. In the HIV clinics, HIV testing was offered to all family members of adults enrolled in care. The ICAP family enrollment genealogy form was used to identify family members including children of adults enrolled in C&T eligible for HIV testing. Eligible children and family members are sent to VCT for HIV testing. We used routinely collected aggregate data to describe trends in HIV testing from August 2007 to July 2011 at 46 ICAP supported facilities. Cochran-Mantel-Haenszel tests was used to analyze trends in the difference in volume and proportion tested and linear regression weighted by number tested to look at trends in proportion testing positive.

Result: Overall children accounted for 16% of the 2,356,462 HIV tests performed over the 4 year period. The proportion of children with unknown status tested in the pediatric inpatient ward increased from 11,851 (73%) in 2007-8 to 22,780 (84%) in 2010-11, (p < 0.0001). Testing amongst children with unknown status in the pediatric OPD also increased; from 33,625 (21%) in 2007-8 to 98,680 (68.5%) in 2010-11, (p < 0.0001). The proportion testing positive in both the pediatric inpatient wards and OPD decreased over time from 3.0% to 0.8% (p=0.047) and from 2.8% to 0.4% (p=0.159) respectively. PITC among children of adults in C&T had the highest yield testing HIV positive; 13.3% in 2007-8 and 5.7% in 2010-11. Over the four year period the total number of clients enrolled in care was 52,121 with children accounting for 4459 (8.6%). Pediatric enrollment into care from the testing venues increased over the four year period; from 63.8% to 76.5% in the inpatient ward (p<0.0001); 64.5% to 87.9% in the OPD (p<0.0001); and 80.7% to 81.3% at VCT (p=0.41).

Conclusions: Scale up of PITC resulted in a significant increase in the proportion of children tested for HIV at both the OPD and pediatric inpatient wards. However, there has been a decrease in seroprevalence in children overtime. Besides strengthening PITC, there is a need to look closely at optimal strategies for testing children in low seroprevalence countries.

No conflict of interest
Abstract: P_31

Comprehensive Pediatric HIV care

Vascular Inflammation and Body Fat are Associated with Resting Energy Expenditure in HIV-Infected Children

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Background: Changes in energy metabolism can contribute to altered nutritional balance in HIV-infected children (HIV+). Resting energy expenditure (REE), one component of energy balance, can be increased because of an HIV-induced chronic inflammatory state or during opportunistic infections. Alternatively, loss of lean tissue can result in lower REE. Vascular inflammation has been reported previously in pediatric HIV, however, the extent to which these inflammatory changes are associated with altered energy expenditure is unknown.

Objective: We sought to determine the differences in REE between HIV+ children and non-HIV-infected controls. We also determined demographic, clinical and biochemical factors associated with increased REE amongst HIV+ children.

Material & Methods: Children enrolled in an NHLBI-sponsored prospective study of cardiac risk factors in HIV-infected children from 2009-2012 were considered for this cross-sectional analysis. The first visit from this longitudinal study was used for children who had simultaneous measures of REE and biomarkers associated with vascular inflammation. REE, the main outcome, was measured in kcal/kg-lean body mass per day (LBM). Covariate vascular biomarkers included: C-reactive protein (CRP), fibrinogen, interleukin-6 (IL-6), leptin, monocyte chemo attractant protein-1 (MCP-1), soluble E-selectin, soluble P-selectin, soluble vascular cell adhesion molecule (sVCAM), and soluble intracellular cell adhesion molecule (sICAM). Demographics, anthropometry (height, weight, body mass index (BMI)), body composition (percent body fat), fasting lipids, HIV disease severity (CD4 counts and viral load), and antiretroviral therapy were also recorded as additional covariates. Outcomes and covariates were compared using t-tests and Fisher’s Exact tests. Adjusted comparisons were evaluated using linear regression analysis. A multivariate model analysis determined predictors of REE.

Results: Ninety-nine HIV+ and 37 controls were included in the analysis. The mean ages were 15.7y (HIV+) and 13.3y (controls) with an equal distribution of ethnicity and sex. The mean absolute CD4 count was 571 (range: 7-2136) and 49% of HIV+ had viral loads under 400 copies/mL. Age, sex and ethnicity-adjusted heights, weights, BMI, and LBM were non-significantly lower in the HIV+ versus control, although HIV+ had a higher percent LBM (74.2% vs. 68.0%, p=0.04). REE adjusted for age, sex, and ethnicity were similar among HIV+ compared to controls (0.84 kcal/kg-LBM, p=0.95). A bivariate adjusted analysis showed that MCP-1 [HIV+ 128.8 (5.3) vs. controls 108.2 (7.9)] and sICAM [HIV+ 261.2 (13.4) vs. controls 192.4 (19.8)] were significant predictors of REE, as represented by their means and standard errors, respectively. A multivariate model adjusting for age, sex, and ethnicity showed sICAM (estimate +0.0006; p=0.01) and leptin (estimate -0.014; p=<0.0001) are independent predictors of REE (kcal/kg-LBM) in this HIV+ cohort (R²=0.62). No HIV-specific variables were associated with REE (CD4, viral load).

Conclusions: HIV+ children have similar REE compared to controls. Higher levels of leptin, often correlated with higher body fat, were associated with lower REE. Biomarkers that reflect vascular inflammation are also associated with higher REE. As HIV+ children develop a greater tendency for obesity, lower energy requirements may need to be considered.

No conflict of interest
Abstract: P_32

**Comprehensive Pediatric HIV care**

**Critical Gaps and Reasons for Delayed ART Initiation and Poor Retention in Uganda's National Pediatric ART Program**

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**Introduction:** Scale-up of Uganda's Pediatric ART program resulted in 21,000 children on ART in 2010 (28% coverage). Little is known about barriers to retention and survival of these children. The Ministry of Health, in collaboration with Clinton Health Access Initiative (CHAI), undertook a study to quantify attrition and identify the drivers of loss throughout the pediatric HIV care continuum.

**Methods:** A retrospective cohort was selected using systematic random sampling (HIVQUAL sample size model) from among 1122 HIV+ children < 15 years from 10 facilities across Uganda from Jan07-Nov10. Data were collected from patient files, registers, interviews with health workers and observation of clinic systems.

**Results:** 532 HIV+ children (median age 5 years) enrolled in care before November 2010, were selected from 3 hospitals (176), 5 Health Centre IV (250) and 2 Health Centre III (106). Only 66% (181/276) eligible children initiated ART, with mean delay from eligibility to initiation of 6.9 months (n=159); Early Infant Treatment was a challenge with only 62% (23/37) of HIV+ infants initiated on ART; half of those not initiated were lost. Overall 60% (n=340; range 23-96% across facilities) of the children enrolled before July 2009 were active in care by November 2010. Retention for pre-ART children was 45% (n=193), versus 80% (n=147) among ART children. One third of pre-ART Loss occurred in the first 6 months in care. Only 57% (31/54) of children enrolled in the previous 6 months received a CD4 test. Fragmented clinic systems, poor linkages/ follow up, health worker knowledge gaps, inadequate mentorship and poor data management were identified as drivers of loss.

**Conclusions:** This National Paediatric HIV review identified critical gaps and led to implementing interventions to improve retention and quality of care. These include improved training/mentorship curricula, revised data tools and job aides, phone follow-up and strengthening Pre-ART services. A follow-up survey is planned.

No conflict of interest

Abstract: P_33

**Comprehensive Pediatric HIV care**

**The Effects of Transportation Vouchers on Attendance Rates of Pediatric HIV Patients at the DARDAR Pediatric Program: A Randomized Cross-Over Study**

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**Introduction:** Despite advancements in antiretroviral therapy for HIV infection, maintaining strict treatment adherence remains challenging. Transportation limitations, including distance to care and high travel costs, are well-documented barriers; currently, a cost-effective solution has yet to be identified. In this study, we evaluated the efficacy of using transportation vouchers to improve adherence to scheduled appointments for HIV-infected pediatric patients in Tanzania.

**Materials & Methods:** All HIV-infected children enrolled at the DARDAR Pediatric Program (DPP) in Dar es Salaam, Tanzania were eligible.
Forty-eight subjects (ages 3-16) were randomized and evenly distributed into two groups (A and B) in a non-blinded, cross-over study from Feb-Nov 2010. Transportation vouchers (TV) valued at 5000 Tanzanian Shillings ($3.80) were distributed to eligible patients who attended their appointment 'on-time' - defined as receiving care on their scheduled appointment date. During the first four months, Group A subjects received TV for each on-time appointment, while Group B subjects were not eligible. Halfway, the two groups were crossed-over. Primary study endpoints were overall on-time attendance rates and attendance rates between the two groups. Univariate analyses were conducted using t-test; p-value <0.05 was statistically significant.

Results: In a pre-study chart review conducted in 2008, the on-time attendance rate for all DPP patients was 49.0%. Over the eight month study duration, on-time attendance for the 48 participants was 80.4%. There were no differences in attendance rates between TV recipients and controls (p>0.05). Changes in CD4 counts and weight were also not different between study arms. The top three reasons for missed appointments were forgetting about the appointment, sickness, and insufficient travel funds.

Conclusions: On-time attendance increased 30% compared to pre-study rates. However, a difference in attendance between the two study arms was not found. We hypothesize that study participation and increased surveillance fostered an improvement in attendance even when study participants were not eligible to receive TVs. Further research would benefit from a larger, multi-center study. In conclusion, the use of transportation vouchers may be a cost-effective method to ensure strict treatment adherence; this will lead to better health outcomes, less antiretroviral resistance, and ultimately decreased overall cost of HIV care.

No conflict of interest

Abstract: P_34

Comprehensive Pediatric HIV care

To feed or to nourish? Perspectives of HIV-infected and affected children on feeding practices in their schools

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1Botswana-Baylor Children's Clinical Centre of Excellence, Pediatrics, Gaborone, Botswana; 2University of Botswana, Sociology, Gaborone, Botswana

Background: Although malnutrition is a known HIV/AIDS co-morbidity, its prevalence among HIV-infected children in Botswana is unknown. We carried out a nutritional survey among HIV-infected Batswana children with a view to informing health and education policy.

Methods: We selected a representative sample of children aged 6-12 years from 12 antiretroviral therapy (ART) sites accounting for over 90% of all children on treatment in Botswana. Data were collected using an interviewer-administered questionnaire. Children were eligible if they had documented HIV positive status, they had been fully disclosed to and if their age was 6-18 years. Children's heights in centimetres and weights in kilograms were measured and recorded. Prior ethical approval, informed consent by caregivers and assent by eligible children were prerequisites. Quantitative nutritional data were analysed using WHO AnthroPLUS software.

Results: Of 984 children studied, 98.8% were attending public schools which provided 1-2 hot meals per day. 27.4% of all children reported eating only 1 or 2 meals a day while 13.2% said they had slept hungry the previous night and more than 50% said they felt hungry all the time. Only 42.6% of the children were assessed as eating a regular balanced diet. Most diets were high in starchy foods and contained relatively low protein. The least consumed foods were fruits and vegetables. Of 844 children with evaluable data, 33.5% were stunted (HAZ < -2SD); and 9.5% were severely stunted (HAZ < -3SD). Of 838 children evaluated, 198 (23.6%) were underweight (WAZ < -2SD).
Conclusions: There were poor child feeding practices among the majority of HIV infected children aged 6-18 years. School meals were essential for the survival of many children and so improvements in school diets can impact the nutritional status of these children. These data also suggest that many caregivers have transferred their child feeding responsibilities to schools.

No conflict of interest

Abstract: P_35

Comprehensive Pediatric HIV care

Characteristics of Learning Difficulties (LD) in children identified as poor school performers at a paediatric HIV centre in Gaborone, Botswana

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Background: Learning Difficulties (LD) are a substantial concern for HIV-infected children. Affected children are less likely to complete schooling. In Africa, especially in Botswana, the prevalence of and risk factors for the development of LD in paediatric populations are poorly characterized.

Methods: Retrospective review of clinic psychologist’s records for school-going children aged 7-19 years referred for poor school performance from January, 2008 to December, 2011 was done. Diagnosis of LD was made per Woodcock - Johnson III tests of cognitive abilities (WJ III) with a score < 49% or any below average performance considered as diagnostic. Clinical data was extracted from the Electronic Medical Record (EMR) and associations examined.

Results: Of the 30 patients evaluated, 11(35.48%) were females (M:F ratio 2:1); average age was 12 years (7 years to 17 years). 25 children (83%) had repeated a grade and 10 (30%) had repeated a grade multiple times. All were virologically suppressed and the average CD4 was 1194, 37%. Average hemoglobin (HgB) was 12.8. The most common LD was memory problems (N=29; 97%). Of the 10 who had repeated a grade multiple times, average CD4 was 1229/38%, HgB was 12.6 and all had viral suppression. 20% had ear infections. Of note, all 6 patients with global impairment a had history of ear infections. However, ear infections were not significantly associated with memory problems (p = 1.000).

Conclusions: This is the first study to characterize LD in HIV-infected children in Botswana. While early HIV diagnosis and administration of ART will likely reduce rates of LD in HIV-infected children, there was no association between current immunologic status or virologic suppression and LD in this study. Early diagnosis and treatment of otitis-media is likely to prevent severe forms of LD. Lastly, the WJ III appears to have utility as a LD screening tool in children in Botswana, further assessment would be useful.

No conflict of interest

Abstract: P_36

Treatment of pediatric HIV infection

The Strategic Multisite Initiative for the Identification, Linkage and Engagement to Care of HIV-Infected Youth (SMILE): Can Treatment as Prevention Work for American Minority Youth?

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1National Institute of Child Health and Human Development, Pediatric, Adolescent and Maternal AIDS Branch, Bethesda, MD, United States; 2Indiana University School of Medicine, Pediatrics, Indianapolis, IN, United States; 3Westat, Rockville, MD, United States; 4Johns Hopkins University,
**Background:** The National HIV/AIDS Strategy emphasizes the importance of linkage to care (LTC) for newly diagnosed persons. HIV incidence has increased by 48% among gay minority youth since the first CDC estimates in 2008. Up to 80% of HIV+ adolescents and young adults are unaware they are infected and, based on recent sexual debut, are more likely to be recently infected. Such dynamics are likely central to facilitating HIV transmission, yet no comprehensive national-level data exist on LTC efforts or community viral loads (VL) within youth.

**Methods:** SMILE in Caring for Youth (SMILE) is an NIH, CDC and Adolescent Medicine Trials Network for HIV/AIDS Interventions (ATN) collaboration to determine factors associated with LTC program effectiveness across 15 U.S. ATN sites. Numbers of HIV-positive youth referred, linked (≤42 days of referral), and engaged (≤16 weeks of linkage) in care were recorded along with demographics, case dispositions, and reasons for failure in care linkage/engagement. Baseline HIV VL and CD4 cell count data were compared by demographics, socioeconomic, risk behaviors, and ATN site using Kruskal-Wallis tests.

**Results:** Since SMILE started in 2010, 1409 HIV+ youth presented for care. Among those, 988 (70.0%) were linked to care and 694 (70.0%) of those engaged in care at ATN sites. Numbers of HIV-positive youth referred, linked (≤42 days of referral), and engaged (≤16 weeks of linkage) in care were recorded along with demographics, case dispositions, and reasons for failure in care linkage/engagement. Baseline HIV VL and CD4 cell count data were compared by demographics, socioeconomic, risk behaviors, and ATN site using Kruskal-Wallis tests.

**Conclusions:** There are significant gaps in identifying and linking youth to care across major US cities. Even among the 70% of the cohort with health seeking behaviors, the opportunity for secondary transmission events is very high. Structural and individual-level interventions are urgently needed to improve access to and retention in care for HIV-infected youth.

*No conflict of interest*

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**Table 1. Reasons for LTC Failure (n = 421)**

<table>
<thead>
<tr>
<th>Reasons for LTC Failure</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unable to Locate</td>
<td>153 (36)</td>
</tr>
<tr>
<td>Repeated Appointment Failure</td>
<td>140 (33)</td>
</tr>
<tr>
<td>Refused LTC</td>
<td>43 (10)</td>
</tr>
<tr>
<td>Out of Jurisdiction</td>
<td>40 (10)</td>
</tr>
<tr>
<td>Other</td>
<td>45 (11)</td>
</tr>
</tbody>
</table>

**Table 2. Community HIV VL in U.S. youth 12 - 24 years (n = 852)**

<table>
<thead>
<tr>
<th>ATN Site</th>
<th>Mean HIV VL</th>
<th>Median HIV VL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Miami, FL</td>
<td>43,415</td>
<td>10,984</td>
</tr>
<tr>
<td>Chicago, IL – Central</td>
<td>49,362</td>
<td>11,531</td>
</tr>
<tr>
<td>Washington, DC</td>
<td>53,297</td>
<td>17,622</td>
</tr>
<tr>
<td>Los Angeles, CA</td>
<td>53,875</td>
<td>11,600</td>
</tr>
<tr>
<td>Baltimore, MD</td>
<td>60,422</td>
<td>15,135</td>
</tr>
<tr>
<td>Bronx, NY</td>
<td>62,538</td>
<td>15,037</td>
</tr>
<tr>
<td>Memphis, TN</td>
<td>68,362</td>
<td>10,200</td>
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<tr>
<td>Chicago, IL – North</td>
<td>75,082</td>
<td>20,842</td>
</tr>
<tr>
<td>San Francisco, CA</td>
<td>91,102</td>
<td>13,597</td>
</tr>
<tr>
<td>Philadelphia, PA</td>
<td>96,812</td>
<td>20,725</td>
</tr>
<tr>
<td>New Orleans, LA</td>
<td>148,490</td>
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<tr>
<td>Tampa, FL</td>
<td>156,845</td>
<td>11,972</td>
</tr>
<tr>
<td>San Juan, PR</td>
<td>163,567</td>
<td>11,299</td>
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<tr>
<td>Ft. Lauderdale, FL</td>
<td>255,823</td>
<td>4,427</td>
</tr>
<tr>
<td>New York, NY</td>
<td>374,920</td>
<td>18,494</td>
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</table>

**Census Region**

<table>
<thead>
<tr>
<th>Mean HIV VL</th>
<th>Median HIV VL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Midwest</td>
<td>65,690</td>
</tr>
<tr>
<td>West</td>
<td>72,877</td>
</tr>
<tr>
<td>South</td>
<td>91,061</td>
</tr>
<tr>
<td>Northeast</td>
<td>123,853</td>
</tr>
<tr>
<td>Puerto Rico</td>
<td>163,567</td>
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</table>

**Linkage Status**

<table>
<thead>
<tr>
<th>Mean HIV VL</th>
<th>Median HIV VL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Linked to Care</td>
<td>83,481</td>
</tr>
<tr>
<td>Failure to Link</td>
<td>95,255</td>
</tr>
</tbody>
</table>
Abstract: P_37

Treatment of pediatric HIV infection

Outcomes of third-line antiretroviral therapy containing darunavir, etravirine or raltegravir in Thai children with HIV infection


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Background: The number of children requiring third-line therapy is increasing worldwide but treatment outcomes data are limited particularly from the developing world.

Methods: This is an ongoing observational study enrolling HIV-infected children ages 2 to 18 years old from 8 tertiary care hospitals in Thailand who require darunavir, etravirine or raltegravir for triple class (NRTI/NNRTI/PI) failure or toxicity to PI in the current second-line regimen. Children are followed every 12 weeks for 48 weeks.

Results: Forty-four children were enrolled; 35 had triple class failure and 9 had hyperlipidemia to PI in the second-line regimen. Twenty-four were male. At time of switching to third-line regimen, the median age (SD) was 13.5 (2.3) years old. All were on second-line PI with the majority (89%) using lopinavir/ritonavir. Genotyping in 35 children showed M184V (57%), >4 TAMs (26%), NNRTI mutation (74%) and >6 lopinavir mutations (31%). The third-line regimen contained a mean of 4.5 drugs with darunavir in 40%, darunavir in 32%, etravirine in 23%, and raltegravir/darunavir±etravirine in 5%. There was one death, one loss to follow-up and one ART discontinuation. After a median time (SD) of 16 (6.8) months on third-line therapy, the median CD4 (SD) increased from 18 (9)% to 23 (7)% and 488 (305) to 689 (318) cells/mm3. The HIV RNA declined from 3.8 (1.4) to 2.1 (1.0) log10 copies/ml with 75% achieving HIV RNA below 50 copies/ml. The median triglyceride (SD) reduced from 259 (328) to 169 (80) mg/dl. Ten (23%) had HIV RNA above 1000 copies/ml due to poor adherence.

Conclusions: Third-line therapy containing darunavir, etravirine or raltegravir was effective in Thai children; however, it requires close adherence and HIV RNA monitoring as almost one-fourth failed from poor adherence. It is important to develop drugs that would allow for simplification of third-line therapy in children.

No conflict of interest

Abstract: P_38

Treatment of pediatric HIV infection

Two-year treatment outcomes of efavirenz-based first line regimen among South African children genotyped for CYP2B6 516G>T polymorphism

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Background: The efficacy and safety of efavirenz (EFV) have been investigated and well established in numerous clinical trials. EFV-based regimens are recommended for first line antiretroviral treatment (ART) in children >3 years in South Africa. Various factors influence the efficacy of ART with pharmacokinetic (PK) variability of drugs, adherence and viral resistance identified as the most important. We evaluated the influence of the single nucleotide change 516G>T on the treatment outcomes of an EFV-based regimen during a two-year follow-up study.

Method: A cohort of 60 black children, both genders, with no prior exposure to ART, eligible for ART, was enrolled and followed up at Harriet Shezi Children’s Clinic, Chris Hani Baragwanath Hospital, Soweto, South Africa. Viral load (VL), CD4-cell count, CD4% were assessed at baseline, 3, 6, 12, 18 and 24 months and EFV PK assessments were performed at 1, 3, 6, 12, 18 and 24 months post-ART initiation.

Results: 89% (47/53) of the participants were virally suppressed (VL< 25 copies/ml) at 24 months post-ART. There were no significant differences between the three genotyped groups (G/G; G/T; T/T) with respect to the VL; CD4-cell count or the CD4% at baseline (K-W, p> 0.5). Repeated measures ANOVA showed neither genotype nor the interaction (R1*genotype) influenced (p>0.05) the CD4-cell counts or CD4% during the 24 month follow-up whereas CD4-cell counts and CD4% improved with duration of treatment. The majority of the participants already had VL<25 copies/ml at 3 months and there were no significant differences between the groups subsequently.

Conclusions: The efficacy of this EFV-based regimen was not altered by the genotyped groups. All groups showed similar improvement in their immunological (CD4-cell count and CD4%) markers and reduction in VL over the 24 months post-ART initiation despite the fact that the plasma EFV levels showed distinctive differences among the three genotyped groups.

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Abstract: P_39

Treatment of pediatric HIV infection

High-dose vitamin D3 supplementation in children and young adults with HIV/AIDS: safety and efficacy

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Introduction: Vitamin D (vitD) insufficiency is common in people with HIV/AIDS, and may be due to many risk factors. VitD may improve immune status, growth, bone, muscle function, and inflammatory state. The objective is to describe the safety and efficacy of high-dose vitamin D3 (D3) supplementation in children and young adults living with perinatally acquired and behaviorally acquired HIV/AIDS.

Materials & Methods: Safety and efficacy of two high doses of oral daily cholecalciferol (D3) supplementation (4000 or 7000IU/d) was evaluated in 44 subjects (9 to 24 y) with perinatally (PA) and behaviorally (BA) acquired HIV over a 12-week period. Efficacy was defined as serum 25(OH)D (25D) ≥32 ng/mL, and safety as serum calcium (Ca) within normal range and 25D <160ng/mL. Height (HAZ), weight (WAZ) and BMI (BMI) Z scores were calculated. Also assessed: 1,25(OH2)D (1,25D), parathyroid hormone (PTH), ionized Ca, serum albumin, phosphorus (Phos), magnesium (Mg), urinary Ca/creatinine ratio (Ca/Cr), HIV RNA(log) viral load, and HIV treatment status (whether on HAART).

Results: Subject characteristics were 43% PA, 68% male, 75% African American, 18.7±4.7 y, 82% on HAART, and RNA(log) 1.60 to 4.91: 53% had detectable (>1.6) viral load. Serum 25D, low at baseline (4.4-33.6 ng/mL), significantly (p<0.001) increased with D3
supplementation in both the 4000IU/d group (17.9±8.5 baseline, 40.8±13.2 at 6 weeks, 43.0±14.6 ng/ml at 12 weeks) and the 7000IU/d group (20.7±6.1 baseline, 51.3±13.5 at 6 weeks, 51.4±21.4 ng/ml at 12 weeks): 77% and 95% had 25D >32 ng/mL at 6 weeks, and 76% and 86% at 12 weeks with 4000 and 7000IU/d D₃, respectively. 1,25D increased from 45.6±21.0 to 75.2±45.3pg/ml (p=0.001) in the 4000IU/d and from 48.1±20.6 to 66.8±32.1pg/ml (p=0.01) in the 7000IU/d group by 6 weeks. PTH declined in the 4000IU/d group at 12 weeks (from 27.8±12.3 to 20.8±14.5pg/ml, p=0.01). Compared to subjects with undetectable viral load, the 12-week increase in 25D was significantly less in subjects with detectable viral load (+15.7±3.6 vs. +37.1±21.1 ng/ml, p=0.008). 25D did not differ by age, gender, BMI Z score, HIV treatment status, or PA vs. BA. Serum and ionized Ca, Ca/Cr, and albumin stayed within reference ranges for both dose groups. No subjects had increased serum Ca and 25D level >160ng/mL. Other safety measures including serum albumin, Phos and Mg were unremarkable and did not change over the 12-weeks of D₃ supplementation.

Conclusions: Daily oral high-dose D₃ supplementation of 4000 or 7000IU/d was safe and significantly improved vitD status in children and young adults with HIV over 12 weeks. A dose response in serum 25D was evident. Response to D₃ was similar regardless of mode of HIV acquisition.

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Treatment of pediatric HIV infection

Peripheral blood immunologic markers in children and young adults with HIV/AIDS: changes with high-dose vitamin D₃ supplementation

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Introduction: Vitamin D (vitD) affects immunomodulatory and anti-infective activity in several biologic systems. The effect of high-dose vitD supplementation on immunologic markers in HIV/AIDS is explored.

Materials & Methods: Serum 25(OH)D (25D) and immunologic markers were assessed in a safety and efficacy study of high-dose oral daily cholecalciferol (D₃) supplementation (4000 or 7000IU/d) over 12 weeks in 39 subjects (9 to 24 y) with perinatally (PA) and behaviorially acquired (BA) HIV. HIV RNA(log) viral load (VL) and treatment status (on HAART or not), white blood cell (WBC), absolute lymphocyte (ALC), populations of CD4, NK and HLA-DR lymphocytes were assessed, expressed here as % total lymphocytes.

Results: Subjects were 46% PA, 67% male, 77% African American, and 18.3±4.8 yrs: 55% had detectable viral load (RNA(log)>1.6), and 82% were on HIV medications. 25D was low at baseline (4.4 to 33.6ng/mL) and increased from (mean±SD) 19.0±7.5 to 47.6±19.2ng/mL (p<0.001) after 12 weeks of D₃ supplementation: ~80% achieved sufficient vitD status (25D≥32ng/mL) by 12 weeks. VitD status improved in both PA and BA groups and whether or not subjects were on HAART. Improvement in
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vitD status was accompanied by a significant increase in CD4% (from 30.8±11.3 to 33.2±13.0, p=0.01) and decreases in VL (2.6±1.1 to 2.4±1.0, p=0.02), NK% (9.0±5.7 to 7.6±4.8, p=0.01) and HLA-DR% (28.8±14.4 to 24.3±13.8, p=0.03) from baseline to 12 weeks. WBC and ALC changed over the 12 weeks. At both baseline and 12 weeks, VL was significantly negatively associated with CD4% and NK% (p<0.01), and HLA-DR% was positively associated with VL and negatively with CD4%. At 12 weeks, 25D was negatively associated with VL and HLA-DR%. Subjects on HAART had lower VL and HLA-DR%. Among all subjects, CD4% and VL remained constant or improved, indicating the safety of high-dose D3 supplementation. For subjects on HAART, CD4% and VL improved significantly, possibly due to improved adherence to HAART during the study.

Conclusions: Twelve weeks of daily high-dose D3 supplementation improved vitD status regardless of mode of HIV acquisition. CD4% increased and viral load decreased, as did HLA-DR%, a marker of immune activation over the course of the study, particularly for subjects on HAART.

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Abstract: P_41

Treatment of pediatric HIV infection

Pharmacokinetics of 100/25 mg lopinavir/ritonavir tablets in children when dosed twice daily according to FDA weight bands

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Background: Lopinavir/ritonavir (LPV/r) is recommended by European and American guidelines as part of combination antiretroviral treatment for HIV-infected children. Half strength tablets (LPV/r 100/25 mg, Kaletra®/Aluvia®) are approved by the FDA and EMA. LPV/r dosing is based on body weight bands under FDA approval, and body surface area by the EMA. This can lead to differences in number of tablets recommended for some children, and is undesirable from a global access perspective. Also, FDA recommended weight band dosing has been derived from pharmacokinetic modeling but not formally studied in the target population. To confirm the FDA weight band based dosing recommendations, we evaluated the pharmacokinetics (PK) of LPV/r, administered twice daily using half strength tablets.

Materials & Methods: This PK study is part of the ongoing PENTA18 trial (KONCERT), in which children, with fully suppressed HIV viral load (<50 copies/mL) for more than 6 months, are randomized to receive LPV/r twice or once daily, according to FDA weight bands. Full PK assessment of LPV/r was conducted before randomization while children were taking the half strength tablets twice daily. Samples were taken at t=0, 2, 4, 6, 8, 12 hours after observed intake, with or without food. It was planned that the first 16 children enrolled in each weight band would participate in the PK study: 15-25kg (lower, 2 tablets); ≥25-35kg (middle, 3 tablets); >35kg (highest weight band, 4 tablets). LPV and RTV concentrations were determined by HPLC. PK parameters were calculated by non-compartmental analysis using WinNonLin version 5.3.

Results: Seventeen, 16 and 18 children were enrolled in the 15-25kg, ≥25-35kg and >35kg weight bands, respectively. All children had evaluable PK. 22 (43%) children were male and median age (interquartile range) was 10.8 (8.7-14.6) years. Twenty-eight children were from Asian origin, 6 were white, 14 black-African, 2 mixed black/white and one had another ethnic origin. Geometric mean (95% CI) AUC0-12 for...
LPV for the lower, middle and highest weight band were 104.1 (84.9-127.5), 116.9 (100.6-135.8) and 101.9 (87.8-118.3) hr*mg/L, respectively. LPV C\textsubscript{int} values were 4.2 (3.1-5.8), 5.1 (3.5-7.4) and 5.4 (4.0-7.1) mg/L, respectively. There were no significant differences in PK parameters between the weight bands (Kruskal-Wallis, p>0.2). Two children had a trough level below 1.0 mg/L, one in the lower and one in the middle weight band receiving a LPV dose of 9.8 mg/kg and 11.5 mg/kg, respectively.

Conclusions: Lopinavir pharmacokinetic parameters were not significantly different between the FDA weight bands. Mean AUC and trough concentrations were higher than historical pediatric data of LPV/r solution and soft-gel capsules, but similar to adult data reported for tablets. Weight band based dosing recommendations provide adequate exposure when using the half strength tablets.

No conflict of interest

Abstract: P_42

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24-month immune recovery according to age and CD4 percent at initiation of antiretroviral therapy in the IeDEA paediatric West African Cohort (pWADA).

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Background: The question of when to start antiretroviral therapy (ART) in HIV-infected children > 2 years remains unclear. We aim to describe the effects of age and pre-ART CD4% on the immune response after 24 months of first-line ART in West-African children.

Methods: CD4% evolution over 24-month after ART-initiation was analysed according to pre-ART age and CD4% among HIV-infected children <16 years, and enrolled between 2003 and 2009 in the IeDEA paediatric West African cohort. CD4% was monitored at baseline (within 3 months) then every 6 months (± 12 weeks) over 24 months. CD4% change over 12 and 24 months of ART was estimated using multivariate linear mixed models, adjusted for baseline age, initial CD4%, gender and ART regimen. Loss-to-follow-up (LTFU) was defined as any patient with last clinical contact >3 months before the database closing date.

Results: Characteristics at baseline of the 1827 eligible children are as follow: 46% were <5 years of age and 60% presented severe evidence of immunodeficiency according to the 2006 WHO guidelines; 54% were males and 31% initiated PI-based ART. The overall median length of follow-up was 12 months [IQR: 0 – 26]. A total of 1427 children (78%) remained in care for at least 24 months; the remaining 330 either died (5%) or were LTFU (17%). The median number of CD4 measurements was 2 (IQR=1-4), the median CD4% at baseline was 15 (IQR = 8-22) and 21 (IQR=14-27) and 26 (IQR=19-32) at 12 and 24 months respectively. At 24 months, the average CD4% change was significantly lower in children aged > 10 years compared to < 2 years (-4.3%, 95%CI: -7.3; -2.1) and in children initiating a PI-based regimen compared to those initiating NNRTI-based regimens (-3.7%, 95%CI: -5.2 ; -2.1). There was a greater increase in CD4% in severely immunodeficient children at baseline compared to those with no signs of immunosuppression (+6.6%, 95%CI: 4.9 ; 8.3), however, these children did not recover to a level > 25%. We conducted the same model by removing LTFU and deceased patients. Although average CD4 change was slightly higher when considering only children remaining in care, the overall results were similar and there was no statistical difference with the previous observations.

Conclusion: After 24 months of ART, we observed greater CD4% increases in children with greatest degree of pre-ART immunodeficiency, though not reaching complete recovery > 25%. CD4% improved more
Importantly in children initiating ART < 2 years compared to the older ones and in children initiating NNRTI-based ART. Although our results were similar including or not children lost to programme, additional information on deceased and LTFU patients would lead to more accurate estimations. Further modelling is necessary in order to estimate more precisely the immune response to ART in a paediatric population with such high attrition rates.

No conflict of interest

Abstract: P_43

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Efavirenz Exposure in HIV-infected Thai Children Receiving Tenofovir/Lamivudine/ Efavirenz Once Daily

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Introduction: Once daily antiretroviral treatment is favorable for HIV-infected children and adolescents to help improve adherence and quality of life. Studies have reported that efavirenz concentrations are low in children and higher doses maybe are required. We evaluated the steady-state pharmacokinetics of efavirenz prescribed according to conventional weight band dosing guidelines in HIV-infected children.

Methods: Children receiving tenofovir/lamivudine/efavirenz once daily, aged between 3-18 years, weighing ≥15 kg, and virologically suppressed were included in this analysis. Efavirenz was prescribed according to USA-DHHS and PENTA (2009) weight band dosing: 250 mg for 15-<20 kg, 300 mg for 20-<25 kg, 350 mg for 25-<32.5 kg, 400 mg for 32.5-40 kg and 600 mg for >40 kg once daily. Intensive 24-hour blood sampling was performed and efavirenz plasma concentrations determined by HPLC and PK parameters by non-compartmental analysis.

Results: Forty children were enrolled: 17 (34%) were male, mean (±SD) age was 11.7 (3.5) years, and CD4 cell count was 853 (399) cells/mm³. Mean duration on HAART was 354 (155) weeks prior to enrollment. Overall, the median (range) AUC0-24hr was 54.6 (28.0-248.7) mcg.hr/mL and C24h was 1.45 (0.68-10.23) mcg/mL. Pharmacokinetic parameters by EFV dose are shown below:

<table>
<thead>
<tr>
<th>Efavirenz dose (mg)</th>
<th>250 mg (n=4)</th>
<th>300 mg (n=9)</th>
<th>350 mg (n=6)</th>
<th>400 mg (n=9)</th>
<th>600 mg (n=12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUC0-24hr (mcg.hr/mL)</td>
<td>44.9 (41.2-66.2)</td>
<td>55.1 (42.6-248.7)</td>
<td>52.5 (28.0-241.4)</td>
<td>53.2 (44.7-89.3)</td>
<td>59.4 (38.9-99.6)</td>
</tr>
<tr>
<td>Cmax (mcg/mL)</td>
<td>3.51 (2.49-5.38)</td>
<td>3.71 (3.0-11.4)</td>
<td>3.26 (1.77-13.45)</td>
<td>3.46 (2.70-5.75)</td>
<td>4.53 (3.14-6.01)</td>
</tr>
<tr>
<td>C24h (mcg/mL)</td>
<td>1.04 (0.87-1.69)</td>
<td>1.35 (0.74-10.23)</td>
<td>1.46 (0.74-9.35)</td>
<td>1.54 (1.20-2.89)</td>
<td>1.59 (0.68-5.40)</td>
</tr>
<tr>
<td>C24h&lt;1.0 mcg/mL</td>
<td>2/4</td>
<td>1/9</td>
<td>2/6</td>
<td>0/9</td>
<td>1/12</td>
</tr>
</tbody>
</table>

Conclusions: The majority of children achieved adequate drug exposure; however, the percentage of children concentrations below target was higher among children receiving 250 and 350 mg. Higher doses recommended by the WHO in 2010 may minimize the risk of low efavirenz concentrations for children within these weight ranges.

No conflict of interest

Abstract: P_44

Treatment of pediatric HIV infection

Using WHO 2010 dosing guidelines, efavirenz levels remain slightly lower and highly variable in Ugandan/Zambian children weighing 10-<20kg


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Introduction: WHO updated guidelines for weight-band-based efavirenz dosing in 2010, but these have not been evaluated in pharmacokinetic studies. New generic efavirenz tablets, scored once/twice on different sides to provide 200mg/300mg/400mg divided pill doses, also await evaluation.

Materials and methods: Ugandan/Zambian children, weighing 10–<20kg and taking generic double-scored efavirenz tablets plus combination tablets of lamivudine/abacavir or lamivudine/zidovudine were enrolled in a pharmacokinetic sub-study in the CHAPAS-3 trial. The once-daily efavirenz doses were 200mg and 300mg for those weighing 10–<14kg and 14–<20kg, respectively. Intensive pharmacokinetic plasma sampling (t=0,1,2,4,6,8,12,24 hours after observed intake) was performed 6 weeks after ART initiation. Area under the curve(AUC0-24), maximum concentration(Cmax) and trough(C24h) levels were analysed.

Results: 31 Ugandan/Zambian children were enrolled and 29 efavirenz profiles (10–<14kg weightbands (n=11), 14–<20kg (n=18)) were evaluable. 17(57%) children were boys; median(interquartile range) age was 4.6(3.9-5.0) years. The geometric mean(95%CI) AUC0-24 was 46.5(29.4-73.6) and 49.7(30.9-79.9) h.mg/L for weight-band 10–<14 and 14–<20 kg respectively, compared to 58h.mg/L in adults. There was no significant variation in any pharmacokinetic parameters between the weight-bands (rank-sum p>0.6). However, variability was high with CV% 133%, 104% and 156% for AUC0-24, Cmax and C24h, respectively. 9% children weighing 10–<14kg had a subtherapeutic C8h and/or C12h (<1.0 mg/L) and 27% had a supratherapeutic C8h and/or C12h (>4.0 mg/L). 22% children weighing 14–<20kg had a subtherapeutic C8h and/or C12h and 28% had a supratherapeutic C8h and/or C12h (exact p=0.87).

Conclusions: Efavirenz pharmacokinetic parameters in African children 10–<20kg on daily efavirenz using 2010 WHO weight-bands and double-scored tablets, were more variable than data from adults, but similar to previously reported paediatric values, demonstrating the challenges of fixed-dosing when the therapeutic range is narrow. EFV toxicity and ART efficacy data collection is ongoing, alongside acceptability of the double-scored EFV tablet, which has potential to simplify delivery across age-bands from 3 years to adulthood.

No conflict of interest

Abstract: P_45

Treatment of pediatric HIV infection

Antiretroviral Drug Resistance Associated Mutations in HIV-1 Infected Ugandan Children Failing First-line Antiretroviral Therapy

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Introduction: Most national programs in sub-Saharan Africa use World Health Organization (WHO) guidelines to initiate and switch antiretroviral therapy (ART) in HIV-infected children. We investigated the pattern of antiretroviral drug (ARV) resistance associated mutations (RAMs) among HIV-infected Ugandan children failing first-line ART and how these mutations would relate to the World Health Organization (WHO)-recommended second-line regimens.

Methods: We conducted a chart and database review of children at Joint Clinical Research Centre (JCRC) Kampala on ART with virological failure to first-line ART and switched to second-line ART with prior genotypic resistance testing. The pattern of RAMs was determined in frequency runs of the most commonly identified Nucleoside Reverse Transcriptase Inhibitor (NRTI) and Non-nucleoside Reverse Transcriptase Inhibitor (NNRTI) RAMs. Factors associated with accumulation of ≥3 Thymidine Analogue Mutations (TAMs) and K103N were determined using multivariate logistic models.

Results: Of 2570 children provided with ART by December 2010, 210(8.2%) failed first-line and
were switched to second-line ART, 142(67%) of whom with genotypic resistance testing. These 142 children were: mean age 10.9±4.6 years; on ART for 5.9±2.0 years; 79(55.6%) male; 49/103(47.6%), 45/103(43.7%), 5/103(4.9%) and 4/103(3.9%) had HIV-1 subtype D, A, AE and C respectively; 82(57.8%) and 51(35.9%) started on nevirapine and efavirenz based regimens respectively; 67(47.2%) and 73(51.4%) started on zidovudine(ZDV) and stavudine(d4T) containing regimens respectively. The commonest NRTI RAM was M184V, among 126/142(88.7%) children. TAMs were observed among 58/142(40.9%) children with 15/142(10.6%) having ≥3TAMs. The K65R/N mutation which confers resistance to commonly recommended second-line drugs, was observed among 4/142(2.8%) children; while the multi-NRTI resistant mutation Q151M was identified among 3/142(2.1%) children. We observed a borderline significant association between age and accumulating ≥3TAMs (odds ratio (OR): 0.89, 95% confidence interval (CI): 0.79 to 1.01). Children initiated on d4T-containing regimens were 70% less likely to accumulate ≥3TAMs than those initiated on ZDV-containing regimens, OR: 0.30, 95%CI: 0.09 to 0.98, p=0.046. The commonest NNRTI RAM was K103N in 72/142(50.7%) children. Others common were: G190A(n=39(27.5%)), Y181C(n=29(20.4%)), P225H(n=19(13.4%)) and K101E(n=17(12%)). The initial ART regimen (p<0.0001) and history of poor adherence (p=0.0388) were independently associated with accumulation of K103N. Age (p=0.0552) and prior exposure to drugs for prevention of mother to child transmission of HIV (PMTCT) (p=0.0632) had borderline significant association with K103N accumulation. When adjusted for history of poor adherence, age and prior exposure to drugs for PMTCT, children initiated on efavirenz-based regimens were almost six times more likely (Adjusted OR: 5.56, 95%CI: 2.28 to 13.60), p=0.0002) to accumulate K103N when compared to those initiated on nevirapine-based regimens. On the contrary, the Y181C mutation was observed in 26/29 (89.7%) children whose initial regimen was nevirapine-based, and not at all among children whose initial regimen was efavirenz-based (p<0.0001).

Conclusions: NRTI and NNRTI RAMs were common in HIV-1-infected children with virological failure on first-line ART with M184V and K103N most frequent, but the RAMs to the WHO recommended second-line ARVs were rare. Care should be taken to choose the appropriate first-line ART regimens and optimal adherence to ART should be ensured in national programs to minimize the development of RAMs in children.

No conflict of interest

Abstract: P_46

Treatment of pediatric HIV infection

Early Initiation of ART Before 6 Months of Age is Associated with Faster Growth Recovery in Perinatally HIV-infected Children in South Africa

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Introduction: Benefits of early initiation of antiretroviral therapy (ART) on growth outcomes in HIV-infected children initiating treatment during infancy have not been well described. This study evaluates the impact of ART initiation before 6 months of age on growth among HIV-infected children in South Africa followed over 48 months.

Methods: 195 nevirapine-exposed children in Johannesburg, South Africa who initiated ritonavir-boosted lopinavir (LPV/r)-based ART before 24 months of age were randomized to either continue on LPV/r or switch to nevirapine after achieving virologic suppression. For this analysis, children were divided into three groups: those who initiated ART <6 months, 6-12 months, and 12-24 months of age. Weight, height, and head circumference were measured at regular study visits over 48 months post-ART initiation. Age- and sex-adjusted weight-for-age (WAZ), height-for-age (HAZ), BMI-for-age (BAZ), and head circumference-for-age Z-scores (HCAZ) were calculated using World Health Organization growth standards. Locally-weighted scatterplot smoothing was used to generate
curves of WAZ, HAZ, BAZ, and HCAZ over time after ART initiation stratified by age when ART was started. Generalized estimating equations were used to describe predictors of growth outcomes.

Results: 195 children (mean age 10.7±5.9 months), including 54 (27.7%) <6 months, 69 (35.4%) 6-12 months, and 72 (36.9%) 12-24 months old at ART initiation, were evaluated. Prior to starting ART, mean WAZ, HAZ, BAZ and HCAZ and proportions of children underweight, stunted, or wasted were not different between the three groups. After ART initiation, WAZ increased in the first 12 months and then stabilized, BAZ increased in the first 12 months and then declined through 48 months, and HAZ and HCAZ steadily rose through 48 months in the population overall. Children <6 months at ART initiation tended to experience a larger initial increase in WAZ (1.98 vs. 1.44, p=0.084) and HCAZ (1.24 vs. 0.45, p=0.004) in the first 12 months on ART than children 12-24 months at ART initiation. Children <6 months at ART initiation also tended to experience a larger increase in HAZ (1.56 vs. 0.76, p=0.004) between 12 and 24 months on treatment than children 12-24 months at ART initiation. Between 24 and 36 months on ART, children who initiated ART <6 months had a significantly higher HAZ than children who initiated ART 12-24 months (p=0.009). However, by 48 months on treatment there were no significant differences in the attained mean WAZ, HAZ, BAZ, or HCAZ between children <6, 6-12, or 12-24 months at ART initiation.

Conclusions: HIV-infected children initiating ART before 24 months of age and maintained on therapy with adequate virologic and immunologic response experience good recovery in overall growth over 48 months on treatment, with improvements in weight preceding improvements in height. While average weight stabilized near population norm (z-score=0), average height did not attain population norm. Earlier initiation of ART before 6 months of age results in faster growth recovery in HIV-infected children. Our data provide further evidence for the importance of prompt diagnosis and immediate initiation of ART for HIV-infected infants.

No conflict of interest

Abstract: P_47

Treatment of pediatric HIV infection

CXCR4-tropism is associated with the establishment of HIV-reservoir in naïve CD4+ T-cells among HIV-infected Ugandan children receiving ART


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Background: Children have large populations of naïve CD4+ T-cells that characteristically express high levels of CXCR4 and low levels of CCR5, compared to memory CD4+ T-cells. We hypothesized that HIV+ Ugandan children infected with CXCR4-tropic virus would exhibit larger HIV-DNA reservoirs in naïve CD4+ T-cells, compared to children infected with CCR5-tropic (R5) virus.

Materials and Methods: Cryopreserved PBMC from a convenience sample of 12 HIV+ Ugandan children receiving antiretroviral therapy (ART) with undetectable plasma HIV-RNA (<400 copies/ml, Amplicor, Roche) were sorted into naïve (CD27+CD45RA+) and memory (CD27-CD45+ and CD45-CD27±) CD3+CD4+ T-cells. HIV-DNA levels were determined using a Taqman assay targeting gag, normalized to cellular-DNA content (tert, ABI). Co-receptor tropism was determined using a commercial phenotypic assay (Trophile, Monogram). We calculated 1) the ratio of the prevalence of infection (copies per 10⁶ cells) in naïve to the prevalence in memory CD4+ T-cells and 2) the proportion of the total peripheral CD4+ T-cell HIV-reservoir that is contained in naïve CD4+ T-cells, and compared them between children with R5- and dual/mixed(CXCR4/CCR5, DM)-tropic virus using the Kruskal-Wallis Test. All values are reported as median (interquartile range).
Results: Age was 4.9 (3.5-8.1) years, CD4+ T-cell number 743 cells/ul (565-1089), CD4+ T-cell percentage 25 (21-29), and ART duration 95 days (95-147), with 6 subjects each with HIV-envelope-subtypes A and D. R5 virus was identified in 8 and DM virus in 4 children. The prevalence of infection (per $10^6$ cells) among naïve CD4+ T-Cells was 2,962 (129-10,668) for R5-infected children versus 14,733 (1,344-135,120) for DM-infected children (p=0.31). The prevalence of infection (per $10^6$ cells) among memory CD4+ T-Cells was 9,931 (1037-11,808) for R5-infected children versus 930 (151-29,702) for DM-infected children (p=0.61). The ratio of the prevalence of infection (naïve:memory) was 0.7 (0.2-4.3) for R5-infected children vs. 8.9 (6.6-13.0) for DM-infected children (p=0.04). The proportion of the total reservoir that was contained in naïve CD4+ T-cell cells was 53% (25%-80%) for R5-infected children compared to 92% (88%-95%) for DM-infected children (p=0.07).

Conclusion: In ART-treated adults, the vast majority of persistently infected CD4+ T-cells are memory cells. By contrast, we found that a significant proportion of the reservoir resides in the naïve CD4+ T-cells among Ugandan HIV+ ART-treated children. Infection with DM virus was associated with preferential naïve T-cell infection. In developing strategies to eradicate HIV, it will be important to take into account the high levels of naïve T-cell infection in children, particularly among those infected with DM virus.

Conflict of interest financial relationship(s): One author, Wei Huang, works for Monogram Biosciences, the company that developed and offers the Trophile test which determines CCR5/CXCR4 tropism as described in this abstract.

Abstract: P_48

Treatment of pediatric HIV infection

Virologic outcome of second-line antiretroviral therapy in Thailand

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Introduction: Most children in low/middle income settings receive a first-line combination of two nucleoside reverse transcriptase inhibitors (NRTIs) plus a non-nucleoside reverse transcriptase inhibitor (NNRTI) and, at failure, switch to two NRTIs plus a protease inhibitor (PI). It is important to follow children as they grow-up, and assess outcomes of second-line therapy. We estimated the failure rate and assessed risk factors of failure in children on PI-based second-line in Thailand.

Material and Methods: The study population included HIV-infected children on NNRTI-based first-line followed in the Program for HIV Prevention and Treatment (PHPT) multicenter cohort (NCT00433030) whose regimen was switched to a PI-based second-line therapy between April 28, 2001 and January 28, 2010 after failure for any reason. Failure of second-line was defined as either confirmed viral load >400 copies/mL after 6 months of treatment with second-line, death, or switch to a third regimen. We assessed whether the following risk factors at time of switch were associated with failure; sex, age, CD4%, HIV viral load, boosted PI versus neifinavir as second-line, CDC stage, toxicity >grade 1 at switch, NRTI resistance, duration of first-line, and first self-reported adherence after switch. Kaplan-Meier curves and Cox proportional-hazards regression models were used, and a backwards selection procedure determined the factors in the multivariate model.

Results: Five hundred and one children started a first-line NNRTI-based antiretroviral regimen...
and were followed for a median of 6.8 years (IQR 4.8 to 8.3). Of these 501 children, 379 (76%) remained on first-line therapy to the end of their follow-up, 14 (3%) interrupted first-line therapy, and 108 (22%) switched to second-line, including 74 to a two NRTIs plus PI regimen who were followed for at least 6 months on second-line. Thirty-eight (51%) of those 74 children were male and, at time of switch to PI-based second-line their median age was 10.4 years (IQR 6.1-12.8), median viral load 4.0 log10 copies/ml (IQR 3.6-4.7), CD4% 19 (IQR 11-23), and 28% were CDC stage C. All 74 children switched due to virologic failure, and most switched to a boosted PI (n=64, 86%) second-line. Median follow-up on second-line was 4.9 years (IQR: 3.0-7.2). By 2 years, the Kaplan-Meier risk of virologic failure was 38% (95% CI: 29-52%), and this risk increased to 47% (95% CI: 36-60%) by 5 years. In univariate analysis, duration of first-line >2 years (HR=2.0, 95% CI (1.0-4.1), p=0.06) and age >12 years (HR=3.0, 95% CI (1.1-7.8), p=0.03) were associated with failure. After backwards selection, age >12 years was still a predictor of failure in the multivariate analysis (HR 3.1, 95% CI 1.8-8.3, p=0.02).

Conclusions: In this large cohort, over an average of 7 years, about 20% of children required a switch to second-line therapy, and by 5 years on PI-based second-line about 50% experienced failure. As older age predicted failure, intensive adherence counseling may be appropriate at switch and when children reach adolescence. Second-line virologic failure occurred throughout the long follow-up of this cohort, therefore close monitoring of children on second-line is essential.

No conflict of interest

Abstract: P_49

Treatment of pediatric HIV infection

Pharmacokinetics, Safety, and Efficacy of Dolutegravir (DTG; S/GSK1349572) in HIV-1 Infected Adolescents: Preliminary analysis from IMPAACT 1093

Introduction: P1093, is an ongoing, Phase 1/2 open-label PK, safety dose finding study of DTG plus optimized background regimen (children 6 wks to <18 yrs) in age defined cohorts. Selected pediatric doses will be those providing comparable PK exposure to those observed at 50mg once daily in adults with acceptable pediatric safety/tolerability.

Methods: Children >12 to < 18 yrs were enrolled to evaluate DTG weight-based fixed doses at ~1.0 mg/kg once daily. Intensive PK evaluation, over 24 hours, following observed dose (Days 5-10) after DTG was added to stable, failing ARV regimen (or started as monotherapy, those not currently taking ARV). Background therapies were optimized immediately following completion of intensive PK. Safety, tolerability, HIV RNA assessments were performed (Week 4 and every 4 weeks throughout). Target PK exposures were AUC(0-24) range of 37-67 mg*h/mL (primary) and C24 range 0.77 – 2.26 mg/ml (secondary).

Results: Ten adolescents (7 female) with mean (SD) age 14 yrs (1.89) and weight 57.3 kg (17.7) were enrolled. Nine subjects received DTG 50mg and 1 subject received DTG 35mg daily. Median Baseline (BL) CD4+ cell % and HIV-1 RNA log10 were 21.5% (IQR:18.4-26) and 4.40 log10 copies/mL (IQR:4.17-4.84), respectively. DTG demonstrated moderate intersubject PK variability; geometric mean (CV%) AUC(0-24) and C24 were 46.0 (43%) mg*h/ml and 0.90 (58%)mg/ml, respectively. HIV-1 RNA < 40 c/mL was achieved (7/10 subjects (70%)) after 4 weeks of dosing; median change from BL was -

No conflict of interest
2.8log_{10} \text{copies/mL (95\% CI: -3.1, -2.6). DTG was generally well tolerated, with one Grade 3, no Grade 4 AEs, no discontinuations due to AEs, no trends in lab abnormalities.}

**Conclusions:** Preliminary data suggest DTG achieved target mean $AUC_{(0-24)}$ and $C_{24}$ in children $\geq$12 to $<$ 18 years. DTG plus OBT was generally well tolerated (Week 4). Data support further DTG investigation at selected dose, and younger pediatric cohort initiation.

**No conflict of interest**

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**Abstract: P_50**

**Treatment of pediatric HIV infection**

**Changes in NRTI and PI Resistance from 2006 to 2011 in South African Children: Association with Abacavir (ABC) use and Cumulative LPV/r Therapy**

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**Background:** In 2009, South Africa’s National AIDS Council expanded abacavir (ABC) to HIV+ infants/children, which came to effect in April 2010 as a regimen change, replacing stavudine (D4T) as a first-line therapy component. We analyzed the effects of this change on NRTI-resistance mutations in patients when virological failure (VF) occurs and analysed the effect of the cumulative second-line lopinavir/ritonavir (LPV/r) use on emerging protease inhibitor (PI) resistance.

**Materials & Methods:** A validated in-house genotypic assay was used to obtain HIV RT and PR sequences from plasma samples from patients experiencing VF on antiretroviral therapy (ART), which were submitted to the Tygerberg National Health Service Laboratory between 2006 and 2011. Demographic and ART data were obtained from request forms, as completed by the clinicians, submitting samples for genotypic resistance testing. Patients were defined as paediatric when age $<$ 15 years.

**Results:** Between 2006 and 2011, 635 plasma samples were obtained from 557 paediatric patients. ABC use, in tested patients, increased from $<$10\%, in 2006-2007, to 41\% in 2011. This was associated with a temporal increase in L74V from $\leq$3\% prior to 2010, to 5\% in 2010 and 9\% in 2011. When regimens were compared, L74V occurred in 15 (41\%) of 37 ABC/3TC/EFV recipients, 4 (9\%) of 43 ABC/3TC/LPV/r recipients, whereas only 2 received ABC/3TC/NVP of which one had the L74V mutation. Of 191 patients receiving an LPV/r-containing regimen 22 (12\%) had $>=$1 of the following major PI-resistance mutations: V32I, M46I, I47A, I50V, I54V, L76V, V82A/F, I84V, and L90M. Of the 22 patients who failed an LPV/r regimen with PI resistance, 8 (4\% of patients receiving LPV/r) had major Darunavir/ritonavir (DRV/r) cross-resistance mutations (V32I, I50V, and L76V).

**Conclusions:** The increased use of ABC since 2009 has been associated with a marked increased frequency of ABC-resistance (L74V). Compared with ABC/3TC/LPV/r recipients with VF, the risk of harbouring L74V was much higher in patients receiving ABC/3TC/EFV (41\% versus 9\%; $p$=0.001 by Fisher Exact Test). The high frequency of L74V, when patients fail a regimen that contains ABC, especially when combined with an NNRTI, would limit the usefulness of didanosine (DDI) as a second-line therapy component, as L74V confers cross-resistance to DDI. Among 191 LPV/r recipients, 22 (12\%) had genotypic LPV/r resistance and 8 (4\% of LPV/r recipients with VF) DRV/r cross-resistance. The historic use of full-dose ritonavir in infants and patients who received concomitant rifampicin probably contributed to the extensive PI resistance with DRV/r cross-resistance in some patients.

**No conflict of interest**
Abstract: P_51

Treatment of pediatric HIV infection

Prognostic model of mortality for children commencing antiretroviral therapy in Southern Africa: The IeDEA Southern Africa Pediatric Collaboration


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Background: Prognosis of HIV-infected children initiating antiretroviral therapy (ART) in resource-limited settings is not well documented, but is important for planning health service provision and informing treatment guidelines. We estimated prognosis for children starting treatment at pediatric ART sites within the IeDEA Southern Africa (IeDEA-SA) collaboration.

Methods: Children ≤10 years of age initiating ART at IeDEA-SA pediatric sites from 2004-2010 with >1 year of potential follow-up were included. Children transferred to another treatment site or lost to follow-up (LTF) (no visit within 270 days of database closure and not known to be deceased or transferred) before completing 6 months of treatment were excluded. The 11 IeDEA-SA paediatric cohorts were grouped into 5 regions according to geographical area. Crude and adjusted associations of prognostic variables with all-cause mortality during the first year on ART were examined using Weibull proportional hazards models stratified by cohort group. Missing data on prognostic covariates was modeled using multiple imputation. Prognostic models were fit using flexible parametric survival models based on the Weibull distribution. Models with different numbers of parameters were compared using AIC to identify a set of candidate prognostic models. From these, we selected the best model that included CD4% categories (‘model with CD4%’) and another that excluded any measures of CD4 (‘model without CD4%’) since CD4 is not measured at ART initiation in all settings. Final model selection was based on generalizability of the model across different regions, ability to discriminate between groups with good and poor prognosis, and concordance between predicted and observed mortality. Generalizability was assessed using internal-external cross-validation between regions.

Results: Among 10,875 children with 10,204 child-years of follow-up included in the analysis, 8.1% died, 2.5% were LTF and 0.8% were transferred to another facility during the first year on ART. Mortality was associated with younger age, lower CD4%, advanced stage disease, anemia (defined as none/mild, moderate or severe according to US guidelines) and lower weight-for-age z-score (WAZ). The model with CD4% estimated that 1-year cumulative mortality ranged from 1.8% (1.5–2.3) for low risk children (5-10 years old; CD4%≥10%, WHO Stage I/II; WAZ≥-2; No severe anemia) to 46.3% (38.2 – 55.2) for high risk children (<1 year old; CD4%<5; WHO Stage III/ IV; WAZ<-3; Severe anemia). The model without CD4% estimated that 1-year cumulative mortality ranged from 2.2% (1.8–2.7) (5-10 years old; No severe anemia, WHO Stage I/ II disease; WAZ≥-2) to 33.4% (28.2–39.3) (<1 year old; Severe anemia; WHO Stage III/IV; WAZ<-3). The CD4% model was able to discriminate slightly better between prognostic groups compared to the model without CD4%. Agreement between predicted and observed mortality was good for both models with concordance statistics 0.752 (model with CD4%) and 0.744 (model without CD4%). According to the models 57% (model with CD4%) and 58% (model without CD4%) of children were in the low risk group with 1-year mortality <3%.

Conclusion: Both prognostic models showed good discrimination and agreement with
observed mortality. These models will be useful for risk stratification of children starting ART in Southern Africa.

No conflict of interest

Abstract: P_52

Treatment of pediatric HIV infection

Substitutions to initial antiretroviral therapy in children in South Africa – The IeDEA–Southern Africa Paediatric Collaboration

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Introduction: Tolerability, safety and durability of first-line paediatric antiretroviral therapy (ART) regimens are vital to scaling up and maintaining children on therapy. A few paediatric cohort studies in Sub-Saharan Africa have reported on frequency and reasons for drug substitution but there has been no detailed study of ART durability and tolerability in children from the region. We determined the probability of and reasons for stopping/substitution of antiretroviral drugs in the International epidemiologic Databases to Evaluate AIDS, Southern Africa (IeDEA-SA) paediatric data.

Methods: Data from 7 South African IeDEA-SA sites were included in the analysis. All ART-naive HIV-infected children aged <16 years at ART initiation with a documented initial regimen of ≥3 antiretroviral drugs and ≥1 follow-up visit after initiation were included. Follow-up was censored at the first of: first drug stop/substitution, date of death, date of transfer out, date of last visit if lost to follow-up or still in care at database closure. Time to the first treatment stop/substitution was estimated using the Kaplan-Meier method. Predictors of drug stopping/substitution were determined using Cox-proportional hazards models stratified by site.

Results: The median age at ART initiation of 4688 children was 45 (16-84) months with most children being severely ill at ART initiation: 74% had WHO stage III/IV disease and 82% were severely immunosuppressed. Most children (90%) initiated stavudine-based first-line ART, with the most common 'third drugs' being efavirenz (61%) and lopinavir/ritonavir (36%). The estimated probability of stopping/substituting ≥1 drug by 3 years on ART was 20% (18%-22%). The two commonest known reasons for treatment stop/substitution in the 1st and 2nd year were non-compliance (1.1% and 1.3% respectively) and treatment failure (0.6% and 3.5% respectively). Stops/substitutions in the 3rd year were mostly due to toxicity (1.9%) and treatment failure (5.5%).

The estimated probability of stopping/substituting each individual drug by 3 years of follow-up was highest for ritonavir at 66% (59-73%) and lowest for efavirenz at 10% (9-12%). In comparison to children on nevirapine, drug stops or changes for reasons other than treatment failure were more likely for unboosted ritonavir (adjusted Hazard Ratio [aHR] 1.4; 95%CI: 1.0-2.0) and less likely for lopinavir/ritonavir (aHR:0.6; 95%CI:0.4-0.9) and efavirenz (aHR:0.6; 95%CI:0.4-0.8) (adjusted for age, WHO stage, immune suppression, weight-for-age and viral load at ART initiation). Stavudine was less likely to be stopped/changed in comparison to zidovudine or abacavir (aHR: 0.6; 95%CI:0.5-0.8) for reasons other than treatment failure. This may be due to the change from donor-funded programmes with mainly zidovudine-based first-line therapy to state-funded programmes with stavudine-based first-line therapy in keeping with South African National Guidelines introduced in 2004.
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Conclusion: The proportion of children remaining on treatment by 3 years was high at 80% and this may in part be due to lack of alternative paediatric drugs. The commonest reason for stopping/changing ART was treatment failure in the 2nd and 3rd years of therapy while most stop reasons in the first year of therapy are not recorded. In order to understand ART durability better, there is a need to fully ascertain all reasons for changing therapy.

No conflict of interest

Abstract: P_53

Treatment of pediatric HIV infection

Virological failure in HIV-infected children and exposure to prevention of mother to child transmission (PMTCT) in Abidjan, Côte d’Ivoire (pWADA).

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Background: Our study aimed to measure the prevalence of virological failure according to exposure to perinatal PMTCT intervention, in HIV infected children less than 5 years at initiation of antiretroviral treatment (ART), in the Pediatric IeDEA West Africa Collaboration (pWADA) in Abidjan, Côte d’Ivoire.

Methods: In 2011, we conducted a cross-sectional study in the cohort of HIV-infected children on ART included between January 2004 and June 2009 in the pWADA clinical centers in Abidjan. The virological follow-up was not routinely performed in Abidjan. Blood samples of children whose parents gave their consent, had been collected in clinical centers during their clinical follow-up visit over the study period. Viral load was processed at the national laboratory of reference (CEDRES). The prevalence of virological failure (VF) was defined as the proportion of children with a detectable viral load (≥400 copies/ml) at the time of measurement. Logistic regression was performed to access the correlates of VF.

Results: A total of 120 children were included between July 2011 and October 2011, of whom 27 (22.5%) children were previously exposed to PMTCT. At ART initiation, the median age was 31 months (Interquartile range (IQR): 21 months - 46 months) among PMTCT unexposed children and 12 months (IQR: 7 months -27 months) in exposed children (p <0.001). The first-line regimen was NNRTI-based for 43.3% of the children. Their median CD4 percentage was 13.8% (IQR: 10.8% -17.4%). At the time of virological measurement, the median duration of ART was 71 months (IQR: 60.5 months - 78 months); the median age of children was 100.0 months (IQR: 83.5 months – 112.0 months) and their median CD4 percentage was 30.2% (IQR: 22.9% - 36.9%). Overall, the prevalence of VF was 47.5%; 55.6% in children exposed to PMTCT versus 45.2% among unexposed children (P = 0.3). According to the duration of treatment, VF was found in 45.8% of children who had a ART duration less than the median, and in 49.2% of children who had a duration of treatment greater than or equal to the median (p = 0.7). This failure rate remained elevated regardless of the duration of treatment. It was 56.7% for treatment duration less than 60.5 months, 34.5% when the duration was between 60.5 and 71 months, 46.7% between 71 and 78 months and 51.6% for periods greater than 78 months. Previous exposure to PMTCT was not significantly associated to VF (ORa: 1.37; IC95%: 0.49-3.84), p=0.55) when adjusting on other factors (immunodeficiency, clinical stage C, type of Art-regimen and duration of treatment).

Discussion: Our study shows a high prevalence of virological failure in the field conditions of use of antiretroviral drug on children in Abidjan, Côte d’Ivoire independently of PMTCT exposure.
Despite this high rate of virological failure, paradoxically we observed a good immune reconstitution in these children. VL monitoring should be done at least once to adapt the first-line ART if needed in the long-term care of HIV-infected children.

No conflict of interest

Abstract: P_54

Treatment of pediatric HIV infection

Validation of WHO 2010 immunologic criteria in predicting first-line antiretroviral treatment failure in ART-experienced children in Uganda

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Background: Viral load (VL) monitoring is limited in resource poor setting. Treatment failure among HIV-infected children in sub-Saharan Africa is primarily based on immunologic and clinical monitoring. This analysis aims to assess the validity of the 2010 immunologic criteria used to identify treatment failure in antiretroviral treatment (ART)-experienced children.

Methods: HIV-infected children aged 1-12 years with at least 1 year on ART, were screened for a randomized clinical trial comparing clinical and immunologic versus clinical, immunologic, and virologic criteria to identify treatment failure. All children were on NNRTI based first-line therapy and had not met treatment failure criteria according to the 2006 ART guidelines. This analysis used CD4 cell counts and viral loads obtained at baseline of the RCT. Viral load >5000 copies/ml was used to define virologic treatment failure. Sensitivity/specificity and positive (PPV)/negative predictive value (NPV) of CD4 count/percent was evaluated using various CD4 cell cut offs to determine treatment failure, including those set by 2010 ART guidelines.

Results: This analysis included 142 children on NNRTI based first-line ART. Median age was 7 years (IQR 5-9); with 44.4% female. Seventy-nine percent were WHO clinical stage 2 and 3. The median duration on ART was 50 months (IQR 30-63). Median CD4 cell percent was 35% (IQR 26-42). Only 29 percent (41/142) had treatment failure with viral load >5000 copies/ml. Median VL was non-detectable or <400 copies/ml (IQR <400 – 11,870). When a CD4 cut off <200cell/mm³ or 10% for children > 2 and <5 years and <100mm³ for children >5years was used to predict virologic failure (VL>5000 copies/ml), the sensitivity was 6.8% (95%CI 1.4-18.7), specificity was 100% (95%CI 96.6-100), PPV was 100% (29.2-100) and NPV 72.5% (95%CI 64.6-79.5). When a CD4 cut off was increased to <200cell/mm³ or 15% for children > 2 and <5 years and <100cell/mm³ for children >5 years, Sensitivity increase to 11.4 % (95%CI 3.8-24.6), while there is no change in specificity, PPV, or NPV. Further if the CD4 cut off is increased to <200cell/mm³ or 20% for children > 2 and <5 years and <100cell/mm³ for children >5years, sensitivity remains at 11.4% and specificity, PPV and NPV reduce to 99.1 % (95%CI 95-100), 83.3% (95% CI 35.9-99.6) and 73.3 % (95%CI 65.3-80.3) respectively. Increasing the CD4 cut off <200cell/mm³ or 15% for children > 2 and <5 years and <200 cell/mm³ for children >5years, sensitivity remained at 11.4% while Specificity, PPV and NPV was 100% (95%CI 96.6-100), 100% (47.8-100) and 73.3% (95%CI 64.6-79.5) respectively. There was no significant improvement of sensitivity when changing the definition of virologic failure to >1,000 copies/ml or >10,000 copies/ml.

Conclusion: CD4 cell monitoring is a poor predictor of ART failure in treatment-experienced children. Strategic approaches to introduce viral load monitoring in ART programs in resource-limited settings are urgently needed.

No conflict of interest
Abstract: P_55

**Treatment of pediatric HIV infection**

**Long-term response to combination antiretroviral therapy in a Latin American population of previously untreated perinatally HIV-infected children**

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**Background:** Combination antiretroviral therapy (cART) has dramatically reduced morbidity and mortality among HIV-infected children and adolescents. Although outcomes of pediatric antiretroviral treatment programmes in low resource settings are comparable to those achieved in North America and Europe, data on effectiveness of cART in children from mid-developed countries are relatively sparse. The current study describes the long term safety and effectiveness of initial cART in the NISDI (National Institute of Child Health & Human Development [NICHD] International Site Development Initiative) cohort of perinatally HIV-infected Latin American children.

**Material & Methods:** The NISDI pediatric observational cohort enrolled HIV-infected children up to 19 years of age from 5 Latin American countries, from 2002-2009. Study visits occurred at 6-month intervals and included medical history, physical exam and laboratory evaluation. Participants eligible for this analysis were antiretroviral therapy (ARV) naïve at study entry, except for prophylaxis for perinatal HIV transmission, defined as any ARV use within the first 16 days of life. Initiation of cART was defined as the first time three or more antiretroviral drugs from ≥2 classes were used concomitantly; ARV regimens include two NRTI plus one NNRTI or PI and triple class therapy (1 NRTI plus 1 NNRTI plus 1 PI). Univariate analyses were performed examining the change in selected characteristics from baseline to specific time points up to 48 months post cART initiation using a Wilcoxon signed rank test.

**Results:** Of the 1032 perinatally HIV-infected children, 579 were ART naïve prior to their first cART regimen. ARV exposure for prophylaxis occurred in 29.4% (170/579). Two thirds (66%, 382/579) started on PI-based regimens. The mean age at start of cART was 2.1 (SD 2.8) years. Nearly half (48.4%) of the participants suppressed viral load (VL) after a median time of 178 days on treatment. VL was significantly lower at all time points compared to baseline (p<0.0001). CD4 percent was significantly higher at all time points compared to baseline (p<0.0001). The change from baseline in CD4 percent increased from a mean of 4.3% at 6 months to 12.9% at 48 months. Compared to baseline, height z-scores were significantly higher for all time points up to 42 months. Similarly, weight z-scores were also significantly higher at 6, 12, 18, 36 and 42 months compared to baseline (p<0.06). Hemoglobin (HgB) was significantly higher for all time points up to 30 months compared to baseline; the mean HgB values (g/dl) increased from 10.9 at baseline to 12.4 at 30 months. The mean duration of follow up on initial cART was 31.7 (SD 26.7) months. 50.6% (293/579) of subjects switched to second-line therapy during the initial 48 months on treatment. The cumulative mortality was 1.6% (9/579) during the observation period.

**Conclusions:** Long-term cART in this large cohort of Latin American HIV-infected children and adolescents resulted in sustained restoration of CD4 cell counts, control of viral loads and positive impact on growth parameters.

No conflict of interest

Abstract: P_56

**Treatment of pediatric HIV infection**

**Predictors of HIV-1 slow disease progression among perinatally-infected children in Botswana**

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In this large cohort of Latin American HIV-infected children and adolescents resulted in sustained restoration of CD4 cell counts, control of viral loads and positive impact on growth parameters. No conflict of interest.
Background: Perinatally HIV-infected children display a highly variable rate of progression to AIDS. Data about factors underlying this variable disease progression are sparse. Despite sub-Saharan Africa being home to more than 90% of the world’s HIV-infected children, almost all of the few studies that have examined this important question have been undertaken outside Africa. The objective of this study was to examine predictors of HIV-1 slow disease progression among perinatally-infected children in Botswana.

Materials and Methods: Using a case-control design, cases (slow progressors) and controls (rapid progressors) were drawn from medical records of HIV-1 infected children receiving Antiretroviral Therapy (ART) at the Botswana-Baylor Children’s Clinical Centre of Excellence, an outpatient pediatric HIV-treatment clinic in Botswana, between February 2003 and February 2011. Univariate and Multivariate Logistic Regression were performed to identify independent predictors of slow disease progression and control for confounding, respectively.

Results: 152 cases and 201 controls were enrolled, with baseline ages ranging from 6 months to 16 years. Baseline HIV-1 RNA viral load (VL) below 750,000 was the strongest independent predictor of slow disease progression (adjusted OR: 5.52, 95%; CI: 2.75-11.07; P< 0.001). Other independent predictors were: lack of exposure to single-dose nevirapine and zidovudine through the Prevention-of-Mother-to-Child-Transmission of HIV program (adjusted OR: 4.45, 95% CI: 1.45-13.69; P=0.009) and maternal vital status (alive) (adjusted OR: 2.46, 95% CI: 1.51-4.01; P< 0.001). Baseline CD4, CDC Clinical Category, Gender, Age at presentation, Residence and Caregiver relationship to patient were not significantly associated with disease progression.

Conclusions: According to the results of this study, orphans, HIV-exposed infants, and children with high baseline VL are at highest risk of rapid progression to AIDS. Prioritizing these high-risk children for earliest intervention with ART while delaying ART to lower-risk children may mitigate disease progression while at the same time saving costs. This approach could enable the highly affected, yet impoverished, Sub-Saharan African countries to use their scarce resources more efficiently, making their National Antiretroviral Therapy programs more sustainable.

No conflict of interest

Abstract: P_57

Treatment of pediatric HIV infection

Immunological Recovery in HIV-Infected Children: Differences by Baseline CD4% and Age

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Background: CD4% and age at initiation of highly-active antiretroviral therapy (HAART) have been associated with CD4% restoration. However, there is limited information quantifying the long-term immunological impact of initiating HAART at different thresholds of CD4% or age. Our aim was to estimate CD4% change associated with CD4% and age at HAART initiation. We hypothesized that CD4% and age at HAART initiation would be independent predictors of 4-year CD4% changes.
**Materials & Methods:** HIV-1 infected, HAART-naïve children in Europe and the Americas were enrolled in the PENPACT-1 trial of HAART with a non-nucleoside reverse transcriptase inhibitor versus a protease inhibitor. Data from 209 vertically-infected children followed from 2002-2009 were analyzed for the following outcomes 4 years after HAART initiation: 4-year CD4% and proportion of children with normal (≥10th percentile-for-age) CD4% at 4 years (prevalent normal CD4%). Data from the 162 children with at least mild immune suppression and CD4% <10th percentile-for-age were analyzed for the proportion of children with normal (≥10th percentile-for-age) CD4% at any time within 4 years (incident normal CD4%). Baseline CD4% was categorized according to WHO immunological staging; age was analyzed as a continuous variable. Statistical analysis for 4-year CD4% value was conducted using multiple linear regression, while prevalent and incident CD4% recovery were analyzed by modified Poisson regression on the additive scale with the Huber-White variance estimator. Regression models were adjusted for sex and race.

**Results:** Baseline CD4% was associated with 4-year CD4% (p<0.0001), prevalent normal CD4% (p<0.0001), and incident normal CD4% (p=0.001). Severe immune suppression at HAART initiation was associated with a lower mean 4-year CD4% than advanced [mean difference 3.7 percentage points (95%CI: 0.8-6.5); p=0.01], mild [4.6 (1.5-7.8); p=0.004], and no immune suppression [8.8 (5.9-11.7); p<0.0001)). Fewer children with severe suppression had a normal CD4% at 4 years than children with advanced [prevalence difference 17.6% (95%CI: (-)0.2-35.4), p=0.05], mild [26.5% (7.6-45.3); p=0.006], and no immune suppression [39.1% (25.3-52.9); p<0.0001]. Fewer children with severe suppression had a period of normal CD4% at 4 years than children with advanced [prevalence difference 17.6% (95%CI: (-)0.2-35.4), p=0.05], mild [26.5% (7.6-45.3); p=0.006], and no immune suppression [39.1% (25.3-52.9); p<0.0001]. Fewer children with severe suppression had a period of normal CD4% within 4 years than children with advanced [risk difference 19.7% (95%CI: 2.9-36.6); p=0.02], or mild suppression [33.8% (18.9-48.8); p<0.0001]. Each 5-year increase in age at HAART initiation was associated with a decrease in 4-year CD4% of 3.4 percentage points (95%CI: 2.0-4.7, p<0.0001), a reduction in the proportion of children with a normal CD4% at 4 years by 11.1% (95%CI: 3.63-18.5%, p=0.004), and a reduction in the proportion of children with a period of normal CD4% within 4 years by 17.6% (95%CI: 10.2-25.1%, p<0.0001).

**Conclusions:** CD4% and age at HAART initiation have significant independent associations with 4-year CD4% changes. HAART initiation at higher CD4% and younger ages will result in a substantially higher proportion of children with long-term CD4% restoration.

**No conflict of interest**

**Abstract: P_58**

**Treatment of pediatric HIV infection**

**Clinical and immunological characteristics of children receiving HIV care over time in Burundi, Cameroon and the Democratic Republic of Congo**

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**Introduction:** The availability of data describing children receiving HIV care over time in the central Africa region is limited.

**Materials & Methods:** Data were obtained from a cohort study of 476 HIV-positive children receiving care at four HIV treatment programs in Burundi, Cameroon and the Democratic Republic of Congo as part of the International Epidemiologic Databases to Evaluate AIDS (IeDEA) Central Africa region. We examined clinical and immunological characteristics at enrollment into the IeDEA database and at 0-5.9 months, 6-11.9 months, and 12+ months of follow-up.

**Results:** Of 476 children, the majority were male (51%), age 5-18 years (65%), enrolled at WHO
clinical stage 3/4 (58%), on cotrimoxazole prophylaxis (66%) and antiretroviral therapy (ART) (59%). The median duration of follow-up was 3.8 months for 237 children during the 0-5.9 month time period, 8.4 months for 173 children during the 5-11.9 month time period, and 16.4 months for 128 children during the 12+ month time period. The proportion of children on ART increased over time (59%, 80%, 86%, and 93%) as did the proportion on cotrimoxazole prophylaxis (66%, 89%, 92%, 92%). The proportion of children classified as WHO clinical stage 3/4 decreased over time (58%, 62%, 58%, 45%) as did the proportion of children with CD4 results classified as advanced/severe as per WHO severity of immunodeficiency guidelines (46% of 155, 54% of 83, 41% of 58, 27% of 82). The median age of ART initiation was 6.1 years and the duration of time on ART was 1.7 years. At the end of follow-up, 13 children were known to have died, 5 were lost-to-follow-up, and 6 had moved.

Conclusions: The proportion of children on ART and cotrimoxazole prophylaxis increased over time while the proportion with advanced HIV disease progression decreased highlighting the benefits of care and treatment at these clinics. Our data suggest low attrition though additional resources for earlier screening and better tracking are needed.

No conflict of interest

Abstract: P_59

Treatment of pediatric HIV infection

Primary mutations associated with antiretroviral (ARV) drug resistance in naïve HIV-infected children in Mexico

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Background: Primary of transmitted drug resistance in HIV-1 has been a significant clinical and public health concern with the widespread use of antiretroviral therapy (ART) worldwide. There is limited information on primary resistance in HIV-infected children in our country. This study aimed to describe the presence of primary mutations associated with HIV-1 drug resistance in a population of vertically infected children before the initiation of ART.

Methods: From June 2010 to September 2011, a cross-sectional study was conducted among children (<18 years) ARV naïve. We obtained from clinical records: history ARV mother during pregnancy, gender, age, mechanism of transmission of HIV, clinical stage of disease, viral load and CD4+ T cell count. Plasma samples were assayed with the ViroSeq HIV-1 genotyping system. Sequences of the ARV-naïve patients were submitted to algorithm for transmitted resistance Stanford University.

Results: We included 23 patients. The mean age of patients was 5.5 years (4 mo-12 yr). 60% were male. All patients had acquired the infection through perinatal transmission, which has no history of maternal antiretroviral therapy. Eleven (48%) patients had severe immunosuppression, six (26%) patients had no immunosuppression at diagnosis. The total CD4+ count of these patients ranged from 7-1736 with an average 686 cells/mm3. The viral load in these patients had a range from 2,222 copies/mL to 2,970,713 copies/mL, with an average of 308,207 copies/mL. In 5/23 patients had resistance mutations; 3/23 (13%) of children were resistant to ART drugs in the group of NRTIs, resistance mutations in order of frequency were M184V, K70R and M184I. 1/23 patients (4.3%) had transmitted resistance to the NNRTI with the mutation K103S. 1/23 patients (4.3%) had PI resistance and the mutation of great importance for this group was L90M.

Conclusions: In the present study we found a high frequency of transmitted resistance in the study group. These findings support the
recommendation to perform resistance testing for children before treatment initiation.

No conflict of interest

Abstract: P_60

Treatment of pediatric HIV infection

HIV disease progression markers and treatment of HIV-infected children in Ukraine

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Introduction: Ukraine has one of the fastest growing HIV epidemics in the world, with considerable unmet need for treatment among the adult HIV-positive population. Research into the health and treatment of HIV-infected children in this resource-constrained country, or indeed elsewhere in Eastern Europe, has been limited to date.

Material and methods: Enrolment data on children recruited into the Ukraine Paediatric HIV Cohort Study by November 2011 were analysed. Second-line ART was defined as change of ≥3 drugs simultaneously irrespective of reasons or changing 2 drugs due to treatment failure.

Results: Of the 628 children, 99% had acquired HIV vertically, 53% were female and 99% were born in Ukraine. Median age at enrolment was 6.5 years (range, 1 month–16 years); 21% (n=128) had a prior AIDS diagnosis; current WHO clinical staging was 1: 8% (n=51), 2: 46% (n=281), 3: 30% (n=185) and 4: 16% (n=97) (14, missing). Six percent (26/435) of children were HIV/HCV co-infected and 1.6% (7/433) were HBsAg positive. Overall, 498 children (79%) were receiving ART; median age at initiation was 59.2 months (IQR 32.5, 84.8) and 8.1 months (IQR 3.7, 23.0) among children born before and after 01/01/06 respectively. Of treated children, 64% (319/498) were on their first regimen, most commonly Kaletra-based (n=183), usually with a 3TC+ZDV backbone (n=158); 128 children were on NNRTI-based regimens. Overall 11% (n=53) treated children had switched to second-line, with the remaining 126 (25%) treated children having experienced ≥1 drug substitution. Median time since ART initiation was 70 months (IQR 44, 86) among children on second-line regimens and 29 months (IQR 15, 52) for the remainder (p<0.001). Median duration of first-line regimen was 26 months (IQR 14, 32) among children on second-line regimens. Of 377 children treated for ≥6 months by enrolment and with viral loads available, 69% (n=262) were virologically suppressed (<50 copies/ml) (median CD4% 33%); among the 115 children with detectable viral loads, median was 240 copies/ml (IQR 94, 6166) (median CD4% 31%). Factors associated with non-suppressive ART were sex (AOR 0.61, p=0.03 for females versus males), treatment duration (AOR 0.86, p=0.04 per additional year), living situation (AOR 0.50, p=0.047 for living with other family member(s) versus with mother) and exposure to antenatal HAART (AOR 10.4, p=0.046). 130 children were not receiving ART (median age 4.8 years). Forty-one untreated children were eligible for ART according to WHO guidelines; only 2% of untreated children had CD4 measurements. Overall, 93% of children at WHO stage 3-4 were receiving ART (261/282) and only 68% of children aged 24 months or less (50/73).

Conclusions: The overall coverage and response to ART were good in the Ukraine paediatric population although there was a small group of untreated children who were eligible for ART. Age at ART initiation has substantially decreased over time, reflecting implementation of early infant diagnosis and ART roll-out.

No conflict of interest
Abstract: P_61

Prevention of Mother-to-Child transmission

Emergence of nevirapine (NVP) resistance in HIV-infected breastfeeding infants exposed to extended NVP prophylaxis and maternal HIV treatment


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Introduction: The HPTN 046 trial evaluated the efficacy of extended daily infant nevirapine (NVP) for prevention of mother-to-child transmission of HIV (MTCT) through breastfeeding. All breastfed infants known to be uninfected at birth received daily open-label NVP to 6 weeks of age. Infants who were HIV-uninfected at 6 weeks of age (intent-to-treat group) were randomized to receive daily NVP or placebo up to 6 months of age. Many women and infants in the trial received non-study antiretroviral drug (ARV) regimens outside of the trial for prevention of MTCT or for treatment of HIV infection. We analyzed the contribution of extended NVP prophylaxis and other factors with emergence of NVP resistance in infants who acquired HIV-infection despite ARV prophylaxis.

Materials & Methods: Infant plasma, maternal plasma and breast milk were analyzed for NVP resistance mutations using the ViroSeq HIV Genotyping System. Medians and proportions were used to summarize the data. Two-sided Fisher's exact tests were used to test hypotheses about associations between categorical variables.

Results: NVP resistance was detected in 12 (92.3%) of 13 infants who were HIV-infected by 6 weeks and in seven (28%) of 25 infants in the intent-to-treat group who were HIV-infected at 6 months of age (6/8=75% in the NVP arm, 1/17=5.9% in the placebo arm, P=0.001). Among the 25 HIV-infected infants in the intent-to-treat group, four had mothers who initiated ARV treatment by 6 months (three with a NVP-containing regimen, one with an efavirenz-containing regimen). NVP resistance was detected in all four of those infants by 6 months of age (4/4=100%). In contrast, only three (14.2%) of the remaining 21 HIV-infected infants whose mothers did not initiate ARV treatment developed NVP resistance (P=0.003).

Conclusions: Emergence of NVP resistance in HIV-infected infants is associated with exposure to extended daily NVP prophylaxis and exposure to maternally-administered ARV drugs.

No conflict of interest
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**Introduction:** Zambia has introduced new guidelines for prevention of mother-to-child transmission of HIV (PMTCT) in 2010 which recommends extended nevirapine (NVP) prophylaxis for exposed infants during the breastfeeding period. This study examined its field implementations and feasibility in rural Zambia.

**Methods:** A prospective cohort study was conducted in eleven health centers which provide PMTCT services in Chongwe district. HIV-positive mothers who gave birth from January to December 2011 were included in the study. Face-to-face interviews and focus group discussions were conducted to examine their practices of infant care with focus on NVP administration.

**Results:** Of the 149 HIV exposed infants aged one to 24 weeks, 48 (32.7%) were born to mothers who were on antiretroviral therapy (ART) before pregnancy. One hundred and three infants (69.1%) have received NVP and 89.3% of those reported no missed doses. However, further investigation found that the guidelines were not implemented correctly in approximately half of the cases (50 infants, 48.5%). For example, Among 69 infants aged less than six weeks who have received NVP, 16 infants (23.2%) were reported to have received a daily dose of less than 15 mg. Eight out of 35 infants (22.9%) aged over six weeks were still receiving 15 mg. It was also found that while 10 out of 18 infants (55.6%) aged more than six weeks whose mothers receiving ART were still on NVP, the infants whose mother were not on ART received only six weeks of NVP. Most women with low educational background found it difficult to understand dosages and some could not differentiate between NVP and co-trimoxazole.

**Conclusions:** This study identified the confusions over the extended NVP regimens and incorrect implementations at the field level of Zambia, which require urgent attentions from the programme and policy level.

*No conflict of interest*

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**Abstract: P_63**

**Prevention of Mother-to-Child transmission**

**Willingness of Thai HIV-infected parents to disclose their HIV status to their children**

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**Background:** Sharing a diagnosis of HIV can potentially reduce psychological stress among HIV-infected people. Data on HIV disclosure between parents and children in Asia are very limited.

**Methods:** HIV-affected families with children aged ≥8 years were enrolled from HIV clinics in Bangkok and Chonburi. Willingness and readiness of HIV-infected parents to disclose their HIV status to their children were assessed using self-administered questionnaires.

**Results:** Among 367 HIV-infected parents (male 18.8%, women 81.2%), 0.8% already disclosed their HIV status to their children, 14.7% had not yet disclosed but were willing and ready to disclose, 50.4% were willing but not ready, 33.2% didn't want to disclose, and 0.8% didn't respond. Children included 59 boys and 66 girls. Mean (SD) age was 37.5 (+5.2) years for parents, 12.0 (+3) years for HIV-infected children (n=31), and 11.5 (+4.3) years for HIV-uninfected children (n=94).

Parent’s major concerns for disclosure included fears that the child is too young to understand HIV and to keep it confidential (47%), the child may be afraid of getting HIV from them (19%), and the child may think of parents as bad persons (9%). Age 31-35 years (OR=3.06, 95%CI 1.01-15.66, p=<0.01), being male (OR=5.06, 95%CI 1.55-16.50, p=<0.01), and children’s age >17 years (OR=31.48, 95%CI 10.71-92.57, p=<0.001) were predictors of the willingness to disclose. Age 31-35 and >41 years
Abstract: More than half of HIV-infected Thai parents were willing to disclose their HIV status to their children. When and how to disclose without creating negative consequences were major challenges. Parental HIV disclosure studies and demonstration models are needed to guide recommendations in this field.

Conclusions: More than half of HIV-infected Thai parents were willing to disclose their HIV status to their children. When and how to disclose without creating negative consequences were major challenges. Parental HIV disclosure studies and demonstration models are needed to guide recommendations in this field.

No conflict of interest
Abstract: P_65

Prevention of Mother-to-Child transmission

Use of Mono- and Combined Neonatal Prophylaxis for the prevention of Mother-to-Child Transmission of HIV infection in high risk situations in Europe


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Objectives: To evaluate the use of combination neonatal prophylaxis (CNP) in infants at high risk of mother-to-child transmission (MTCT) in Europe and to investigate whether CNP is more effective in preventing MTCT than one drug prophylaxis in this population.

Design: Individual patient-data meta-analysis, pooling data from 8 observational studies.

Methods: Factors associated with receipt of CNP and with MTCT were explored with logistic regression using data from non-breastfed infants, born in 1996-2010 and at high risk of MTCT

Results: Of 5285 mother-infant pairs included, for 1463 (27.7%) no antenatal or intrapartum (IP) antiretroviral prophylaxis was used, for 915 (17.3%) only IP prophylaxis was used and for 2907 (55.0%) antenatal ART was received but mothers had detectable delivery viral load (VL). Neonatal prophylaxis (NP) was administered to 87.5% infants, of whom 1105 (33.3%) received CNP.

Proportion of infants receiving CNP increased from 19.1% in 1996-2000 to 34.3% in 2006-10 (P<0.0001). Factors associated with receipt of CNP were calendar birth year, lack of elective caesarean section, maternal CD4 count <200/µL, maternal detectable delivery VL, no antenatal ART, cohort and no sdNVP intrapartum. Absence of NP was a risk factor for MTCT (aOR:2.29; 95%CI:1.46-2.59; P<0.0001), but CNP receipt was not significantly associated with different MTCT risk versus one drug NP (aOR:1.41; 95%CI:0.97-2.5;P=0.07), adjusting for other risk factors including preterm delivery, maternal VL, ART receipt and elective caesarean section.

Conclusions: CNP use is increasing in Europe. No difference between one drug and CNP was observed. CNP might be considered in a subgroup of children.

No conflict of interest

Abstract: P_66

Prevention of Mother-to-Child transmission

Effectiveness of the prevention of mother to child transmission program for two regions in northern Tanzania

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Introduction: Over the past years many countries in resource limited settings have scaled up prevention of mother to child transmission (PMTCT) programs. In Tanzania in 2010 70% of pregnant women had access to PMTCT services. Parallel to the PMTCT program exists a national program for early infant diagnosis (EID) using dried blood spot
HIV-DNA PCR (DBS), implemented in 2008. The use of collected indicators from both programs provides data about PMTCT program effectiveness.

**Methods:** This is a retrospective data collection from the National PMTCT Mother and Child Follow-up register in two regions of Tanzania (Arusha and Kilimanjaro) from January 2008 to September 2010. We extracted de-identified data about HIV exposed infants and their mothers who received DBS testing for EID within 75 days after birth including infant age, weight, feeding practice, maternal and infant PMTCT regimen, date and result of first DBS. Then we retrieved regional data about uptake and kind of PMTCT services for mothers for the time period October 2008 to September 2010. By linking these data the effectiveness of the program was calculated.

**Results:** In the two regions in two years of 176,807 pregnant women, 160,085 were tested; 4953 (3.1%) were HIV positive and received PMTCT services. Assuming the same prevalence for 16,722 women not tested, 518 were HIV infected. A total of 1971 (~42% of all) exposed infants had DBS results documented. Using the transmission rates (TR) calculated from the recorded DBS, 79 infants born to women without intervention were infected (TR 15.3%), 169 infected despite sdNVP but 122 averted (TR 8.9%), for combination prophylaxis used 142 were infected but 414 infections averted (TR 3.9%) and 11 infected infants had a mother using combination antiretroviral treatment (cART) but 77 infections were averted (TR 2.1%). A total of 441 infants were infected by day 75 but 613 infections were prevented! Remarkable was as well the shift to cART within the two year observation period (4.7% - 19%). Among exposed infants the proportion of those receiving combination prophylaxis far exceeded those receiving MER over time.

**Conclusions:** Using data from the national registers demonstrates effectiveness of the PMTCT program. Women receiving combination prophylaxis or cART are more likely to have their infants tested early. But efforts are need to further scale up the use of more efficacious regimen and to reach all pregnant women with HIV and the exposed infants for follow-up care.

No conflict of interest

**Abstract: P_67**

Prevention of Mother-to-Child transmission

Maternal Syphilis: An independent risk factor for mother to infant HIV transmission

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**Background:** A high prevalence of syphilis was seen among HIV infected pregnant women enrolled in the six weeks of extended NVP (SWEN) study from Pune, India. Maternal syphilis, if not diagnosed early in pregnancy, may increase the risk of mother to child transmission of HIV (HIV MTCT). This secondary analysis aimed at studying the effect of maternal syphilis on mother to infant HIV transmission rates at 12 months.

**Material & Methods:** Of the 730 HIV infected pregnant women enrolled in the SWEN study, 658 were screened for syphilis using VDRL followed by TPHA and are included in this analysis. A woman was diagnosed infected if she had clinical symptoms and was positive on both VDRL and TPHA. Infants of infected mothers were screened for syphilis clinical presentation and tested using VDRL and TPHA. Infant HIV infection was determined by DNA PCR and confirmed using HIV RNA viral load. Data on several known risk factors for HIV MTCT was collected at baseline and follow-up visits. Cumulative probability of HIV transmission at 12 months was estimated using Kaplan-Meier method. Maternal syphilis, as an independent risk factor for HIV MTCT, was assessed using a Cox-proportional hazards models and was adjusted for maternal CD4, viral load, TB, syphilis, education, antepartum AZT, HAART, antenatal care, mode of delivery, and infant birth weight, SWEN and duration of breastfeeding.
Results: Of the 658 mothers tested for syphilis, 34 (5%) were infected and of these all (100%) received penicillin treatment. Diagnosis of syphilis happened at a median of 7 days prior to delivery with an IQR (-42, 2) days. Of the 34 infants of syphilis infected mothers, 4 (12%) were only HIV infected; 3 (9%) were positive for both VDRL and TPHA, and 4 (12%) were positive for VDRL and TPHA and co-infected with HIV. Of the 7 (21%) infants of syphilis infected mothers who tested positive for both VDRL and TPHA, 6 (86%) received penicillin. The Kaplan-Meier estimate of probability of HIV transmission at 12 months among mothers with HIV-syphilis co-infection was 23% (95% CI: 12% - 43%) and among those with HIV mono-infection was 12% (95% CI: 10% - 15%). The adjusted hazard ratio for maternal syphilis of HIV MTCT at 12 months was 2.34 (95% CI: 1.03 – 5.31) with p = 0.04.

Conclusions: Maternal syphilis was identified as an independent risk factor for HIV MTCT, moreover its presence increases the risk of acquiring HIV infection by almost twice. Among HIV positive pregnant women co-infected with syphilis early diagnosis and treatment of syphilis would help in reducing mother to infant HIV transmission.

No conflict of interest

Abstract: P_68

Prevention of Mother-to-Child transmission

Mortality among Mothers and Children by Maternal HIV Treatment Status in Malawi

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Introduction: In many African countries, HIV-infected women with CD4 cell counts ≥350 cells/mm³ are not eligible for highly active antiretroviral therapy (HAART) based on current WHO criteria. Among those treatment-eligible, not all women initiate HAART due to various barriers. Outcomes among women and their children may vary by maternal HAART eligibility and use. We determined the association between maternal HAART status and mortality among mothers and children.

Methods: We analyzed longitudinal data from 3000 HIV-infected mothers enrolled in a clinical trial in Blantyre, Malawi, from April 2004 to September 2009. All women received intrapartum single-dose nevirapine, except very late presenters. Mothers with CD4 <250 were referred to government clinics for HAART according to national guidelines at that time. Using Kaplan Meier survival curves, we compared survival among mothers and children by maternal HAART status. Women were categorized as not eligible for treatment, eligible and treated, or eligible and never treated, and were followed until death or last study visit. Only infants uninfected at birth were included in the analysis. We used Cox proportional hazards models to identify predictors of infant HIV infection or death, and maternal death.

Results: At delivery, 76% (n=2269) of women had CD4 ≥250 (17% CD4 250-349; 59% CD4 ≥ 350) and >99% were HAART-naive. By 6 months, 251 (8%) women had initiated HAART. Mothers and infants contributed 4743 and 4214 person-years at-risk, respectively. There were 92 deaths during follow-up: 24 among those not eligible for treatment; 26 among those eligible and treated; and 42 among those eligible but untreated. HAART ineligible mothers and their infants had significantly higher survival rates, followed by women eligible and treated. Among those eligible for treatment, maternal HAART was associated with a 46% reduction in child infection or death and a 34% reduction in maternal mortality (adjusted hazards ratio [aHR] 0.66 [95%CI 0.54-0.82] and 0.66 [95%CI 0.43-1.00], respectively) compared to those eligible and treated. Among those eligible for treatment, maternal HAART was associated with a 46% reduction in child infection or death and a 34% reduction in maternal death compared to mothers who were eligible but untreated, or their children. In addition to maternal treatment status, maternal
viral load (aHR 1.49, 95% CI 1.08-2.05) and infant birth weight (aHR 0.38, 95% CI 0.24-0.62) were also significantly associated with child mortality during the first 6 months after birth, based on multivariate analysis. For children greater than 6 months, running water in the household (aHR 0.57, 95% CI 0.36-0.90) and breastfeeding (aHR 0.05, 95% CI 0.01-0.21) were associated with a significant (p<0.05) reduction in mortality among HIV-exposed, uninfected children.

Conclusions: In this analysis, mothers not yet eligible for HAART and their children had the most favorable postpartum health outcomes including the highest survival rates, followed by women who were eligible and treated. Continuation of HAART after breastfeeding for mothers who do not meet current treatment criteria needs careful consideration. Reducing barriers to treatment initiation for HAART-eligible women should be a priority.

No conflict of interest

Abstract: P_69

Prevention of Mother-to-Child transmission

Placental Hofbauer cells limit HIV-1 replication and potentially offset MTCT by induction of immunoregulatory cytokines

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Introduction: Despite readily detectable levels of the HIV-1 (co)-receptors CD4, CCR5 and DC-SIGN on placental macrophages (Hofbauer cells [HCs]), the rate of HIV-1 infection in utero in the absence of interventions is only 7% of exposed infants. During pregnancy complicated by HIV-1 infection, virus-exposed HCs should be readily infectable with properties to disseminate virus and facilitate infection in utero HIV-1 transmission. The reason why in utero transmission occurs rarely is unclear but may reflect the limiting nature of HCs to HIV-1 replication.

Materials & Methods: Here, we examine the replication kinetics of human HCs to the primary isolate HIV-1Bal. We also determined the infectivity of HIV-1-exposed HCs by co-culturing with isolated cord and peripheral blood mononuclear cells [CBMCs, PBMCs]. To understand the limiting nature of HCs to HIV-1 replication, we examined the effect of endogenously secreted cytokines on replication kinetics.

Results: HCs have reduced ability to replicate HIV-1 in vitro (p<0.01) and to infect CBMCs and PBMCs (p<0.001 for both) compared to standard infections of MDMs. Un-stimulated HCs constitutively express significantly higher levels of regulatory cytokines, IL-10 and TGF-β, compared to MDMs (p<0.01), which may contribute to immunoregulatory predominance at the placenta and possibly account for down-regulation of HIV-1 replication and infectivity by HCs. We further demonstrate that these regulatory cytokines inhibit HIV-1 replication within HCs in vitro. HCs also exhibit migratory properties similar to MDMs when stimulated by CCR5 ligands MIP1α and MIP1β. Despite this potential for migration and infectivity, HCs were not detected in fresh cord blood.

Conclusions: HCs have reduced ability to replicate and disseminate R5-tropic HIV-1Bal in vitro and potentially offset MTCT of HIV-1 by the induction of immunoregulatory cytokines. Despite the potential for migration and infectivity, HCs are not present in the neighboring fetal circulation. These results implicate HCs as important mediators of protection at the feto-maternal interface during ongoing HIV-1 exposure. The maternal-fetal interface is a very relevant model to characterize correlates of protection against HIV-1 transmission at a mucosal level, and require further characterization. Defining these correlates may contribute towards effective prophylactic and therapeutic HIV-1 vaccine development.

No conflict of interest
Abstract: P_70

Prevention of Mother-to-Child transmission

Immunological Abnormalities Among HIV Exposed Uninfected Infants of Immunologically Suppressed Mothers in Canada

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Introduction: Recent reports of increased morbidity and mortality from infectious diseases among HIV exposed uninfected (HEU) infants have raised concerns about possible immune dysfunction among them. While previous studies have shown a relative decrease in CD4 lymphocytes among HEU infants, the duration and cause is not clear. The objective of this study was to characterize the immunological status of HEU infants born to mothers exhibiting different degrees of immune suppression and viremia at the time of delivery.

Methods: The Centre maternel et infantile sur le sida (CMIS) mother-child cohort was established in 1987 to follow HIV infected mothers and their infants in Canada. Prospectively collected data on 585 mother-HEU infant pairs was analyzed by infant groups according to maternal level of viremia and CD4 count at delivery. Infant CD4, CD8, CD19% and absolute neutrophil counts were assessed at 2, 6 and 12 months of age, and group-wise comparisons done using Wilcoxon rank-sum test. Linear regression models were constructed to examine the primary association of interest after controlling for confounders.

Results: Median absolute CD4+ T cell counts (cells/mm\(^3\)) at 2 and 6 months of age were significantly lower in HEU infants born to mothers with CD4 counts <350 at delivery (n=139), compared to those born to mothers with CD4 counts >350 (n=321) (median 2480 vs. 2660, p=0.03, and 2376 vs. 2655, p=0.05). This difference was no longer significant at 1 year of age. At 2 and 6 months of age, CD4+ T cell counts were lower in HEU infants born to mothers with viral load >1000 copies/ml at delivery (n=45), as compared with HEU infants born to mothers with viral load <1000 copies/ml at delivery (n=398) (2419 vs. 2695 p=0.06 and 2539 vs. 2655, p=0.04). There were no significant differences in CD8+ T cell or absolute neutrophil count in any age group. In multivariate analysis, maternal CD4 count was the most significant predictor of infant CD4 count at two months of age after adjusting for maternal antiretroviral use, infant antiretroviral use and gender (p=0.005,β=0.51). In a separate model excluding delivery CD4 count, maternal viral load at the time of delivery was the most significant predictor of infant CD4 count at two months of age.

Conclusions: There was a significant difference in absolute CD4+ T cell counts among HEU infants born to mothers with lower CD4 counts and higher viral loads at the time of delivery. Given recent concerns of morbidity and mortality from infectious diseases among HEU infants, immune function and immune responses should be closely examined in this subset of HEU infants.

No conflict of interest

Abstract: P_71

Prevention of Mother-to-Child transmission


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Background: This analysis was conducted to identify gaps along the PMTCT cascade and associated factors that need attention to achieve the MTCT-elimination goals.

Methods: We analyzed data from a national cross-sectional facility-based survey enrolling 10,253 caregivers with infants aged 4-8 weeks attending the first immunization visit using a stratified multi-stage sampling design. Data were collected through caregiver interviews and/or from Road-to-Health cards. HIV testing was offered to all infants regardless of HIV-exposure status.

Findings: Of 9,933 participating mothers, 94% (9,304) reported having antenatal HIV-testing performed during pregnancy; 99% of those received test results. HIV infection was reported in 27% (2,653) of mothers, including those knowing their HIV status before pregnancy; 53% (n=3,579) of HIV-negative mothers whose last HIV test occurred at <32wks gestation were not offered a repeat test. Of all (2,653) HIV-infected mothers, 84% had a CD4 test and 43% received triple antiretrovirals (ARVs); 50% (n=1,327) received both maternal zidovudine (AZT) and newborn nevirapine(NVP)/AZT at birth. 71% (n=482) of HIV-infected mothers with a CD4 count ≤350 cell/µl received triple ARVs. Of known HIV-exposed infants (HEI), 85% (n=2,264) received daily NVP-prophylaxis ≥4wks. Of 2,653 known HEI, 33% were intentionally brought to the immunization clinic for Early-Infant-Diagnosis(EID) /PCR testing at 4-8wks, while 99% of those offered HIV testing at the clinic visit consented to EID. Our data did not show any statistically significant factors associated with low coverage of triple ARVs in women with CD4≤350µl/ml.

Conclusion: We found that repeat testing at 32wks of pregnancy, uptake of CD4 testing, triple ARVs for women with CD4≤350µl/ml, and uptake of EID were gaps along the PMTCT cascade in South Africa in 2011. Offering HIV-testing for all infants is acceptable and could be useful to identify HIV-infected infants early to provide efficacious ARV therapy. The identified gaps should receive attention to achieve the MTCT elimination goals.

No conflict of interest

Abstract: P_72

Prevention of Mother-to-Child transmission

Scale-up of ART as Prevention in PMTCT Settings in Namwala District of Southern Province of Zambia

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Introduction: Nationwide, implementation of treatment for prevention has not yet occurred nor have best practices been established to guide scale-up, though Anti-Retroviral Therapy (ART) guidelines in Zambia emphasize treating HIV positive partners in discordant couples in-line with results of HPTN 052. Joint partner HIV testing and counseling (HTC) is pre-requisite to implementation of treatment for prevention. We describe the status of treating discordant couples in Namwala in 2011 and estimate the potential impact the current treatment program may have and implications of further scale-up through the antenatal (ANC)/prevention of mother-to-child transmission (PMTCT) platform which seems best placed in this initial phase to capture couples.

Methods: We collected 2011 annual PMTCT program data on pregnant women receiving HTC with their partners; number of discordant couples; and number of positive partners in discordant couples initiated on ART. We modeled vertical infections and new adult infections potentially averted by treating...
discordant couples using estimates of data on impact of ART on risk of transmission in discordant relationships (HPTN 052 - 96% reduction), risk of incident HIV in pregnancy (4%), vertical transmission risk in incident HIV during pregnancy (2-3 fold increase), and estimations of expected pregnancies by population.

Results: The district recorded 6504 first ANC attendees in 2011. Of these, 3429 (53%) tested with partners, 100 (6%) of couples were discordant, and 25 (25%) positive partners in discordant couples received ART. Of 66 HIV negative women with positive partners, 26 incident cases are estimated which without intervention, would result in 18 pediatric infections. Of the 100 discordant couples, we estimate 40 new adult cases in a year. With ART, 16 pediatric and 36 adult infections could be averted. If a modest couple HTC coverage of 50% were achieved nation-wide as seems feasible in the Namwala ANC/PMTCT program, we estimate that Zambia could avert 1,300 new pediatric and 3,215 new adult infections, annually in ANC settings.

Conclusions: Implementation of ART for prevention is feasible in ANC/PMTCT settings and could contribute towards attainment of elimination of vertical HIV transmission whilst also averting new adult infections. Our model suggests that nation-wide, implementation of this intervention would avert 14% of MTCT that needs to be averted in order to reach elimination. Despite coverage of partner testing rising in Namwala, thus suggesting feasibility at national level, initiation of positive partners on ART is still low. There is need to investigate for factors associated with non-initiation of ART for prevention purposes where services are available. These results are based on a rural Zambia setting and might not necessarily be applicable in urban settings.

No conflict of interest

Abstract: P_73

Prevention of Mother-to-Child transmission

Masihambisane: An HIV+ community health worker intervention for S. African Mothers Living with HIV improves longitudinal maternal and infant outcomes

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Background: Community Health Workers (CHWs) are increasingly expected to task-share community-level prevention and treatment adherence services. Masihambisane is an intervention for Mothers Living with HIV (MLH) and their infants using HIV+ Peer Mentors to increase PMTCT task adherence, decrease likelihood of having a low birth weight (LBW) infant, improve maternal mental health, and increase implementation of protective behaviors with their partners. Effectiveness was evaluated against standard PMTCT protocol in a RCT.

Methods: In KwaZulu Natal, South Africa, pregnant MLH, aged 18-44 years (M=26.5) were randomly assigned by clinic to either the intervention (n=5 clinics; n= 544 MLH) or standard care (n=4 clinics; n=656 MLH) (i.e., no CHW support). Assessments were conducted during pregnancy (baseline), at post-birth (at approximately 1.5 months), and at 12 months post-birth. MLH in the intervention were invited to attend four ante-natal and four post-natal small group sessions led by an HIV+ Peer Mentor Mother addressing issues such as HIV testing, prevention behaviors, medication adherence, HIV status disclosure, and infant feeding practices.

Results: After controlling for baseline differences and time-varying covariates, we conducted random regression analyses to examine outcomes among MLH and their infants.
from pregnancy to post-birth/12 months post-birth. MLH in the intervention were significantly more likely to get 6-week PCR testing for their infants (adjusted probability, 95.7% vs. 89.9%); less depressed over time (9.8% at baseline, 1.9% at post-birth, 1% at 12 months); more likely to ask their partner(s) to test for HIV (adjusted probability, 70.4% vs. 51.9%, p < .01); and more likely to have infants who achieved better length-for-age z-scores according to WHO Global Health Standards (-0.1 vs. -1.8, p < .05).

**Conclusion:** Small group sessions led by an HIV+ Peer Mentor resulted in increased adherence to preventive behaviors, decreased maternal depression, and better infant outcomes.

*No conflict of interest*

**Abstract: P_74**

**Prevention of Mother-to-Child transmission**

**Philani Plus: A generalist community health worker home-visiting intervention with pregnant women improves maternal and child outcomes in S. Africa.**


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**Background:** There is high co-occurrence of HIV, alcohol use during pregnancy, and child malnutrition in South Africa. The Philani neighbourhood-level home visiting program for maternal and child nutrition was enhanced to also address HIV and alcohol use (‘Philani Plus’). This generalist CHW intervention, delivered by neighbourhood ‘Mentor Mothers’ (MM), was evaluated in a RCT.

**Methods:** In Cape Town, South Africa, 24 matched township neighbourhoods were randomized to the Philani Plus (N=12; n=644 mothers) or standard Philani nutrition program (N=12; n=594 mothers). Mothers and infants were assessed during pregnancy, at one-week post-birth (92% follow-up), and at six months post-birth (88%). MM were recruited from the townships and trained in cognitive-behavioural approaches to problem-solving and skill-building around HIV/AIDS, PMTCT, alcohol use, and nutrition/infant feeding.

**Results:** Mothers Living with HIV (MLH) in Philani Plus were more likely to adhere to the complete PMTCT protocol, including taking maternal anti-retroviral (ARV) medication prior to and during delivery (92% vs. 83%, p=0.01); administering infant ARV during and after birth (91% vs. 82%, p=0.04); using only one feeding method (56% vs. 43%, p=0.003); having fewer birth complications (26% vs. 15%, p=0.04); and having fewer infants 2 SDs below the mean WHO standard for infant length-for-age (17% vs. 26%, p=0.01). The reduction in hazardous alcohol consumption among pregnant women was greater in Philani Plus (19% versus 9% decrease; p=0.02). Among women who previously had a LBW infant, Philani Plus mothers were less likely to give birth to another LBW infant during this study (11% vs. 26%, p=0.04). Finally, Philani Plus mothers were more likely to breastfeed LBW infants for at least 4 months (62% versus 17%; p=0.0003).

**Conclusions:** Paraprofessional MM, trained as generalists to support mothers via home visits, improve maternal and child health outcomes, including HIV treatment adherence.

*No conflict of interest*

**Abstract: P_75**

**Prevention of Mother-to-Child transmission**

**Maternal HIV infection affects ferritin levels in cord blood of HIV exposed, uninfected (HEU) infants**

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Introduction There is increasing evidence that HIV-exposed, uninfected (HEU) infants are experiencing poor growth and increased rates of morbidity and mortality, although the underlying cause for these observations is unclear. Prior research has demonstrated that elevated maternal serum ferritin, an iron storage protein but also a marker of inflammation and oxidative stress, is associated with pregnancy complications and, in HIV disease, with a poorer prognosis. The purpose of this study was to explore potential mechanisms for the poor outcomes of HEU infants by evaluating, in parallel, markers of iron status and inflammation/oxidative stress in maternal and cord blood (CB) of HIV positive (HIV+) and HIV negative (HIV-) women.

Materials and Methods Eighty-seven term, pregnant women (45 HIV+ and 42 HIV-) were enrolled prior to delivery in Kalafong Hospital, Pretoria, South Africa and maternal venous and CB specimens obtained. All infants were later confirmed HIV negative by PCR testing. Standard laboratory methods were used to measure iron status including levels of serum iron, ferritin, transferrin, % transferrin saturation and soluble transferrin receptor (sTfR). CRP, IL-6 and sRAGE (soluble receptor of advanced glycation end-products) were measured as markers of inflammation and/or oxidative stress.

Results HIV+ mothers were significantly older (28 vs. 26yrs, P<.05), but pregnancy and delivery characteristics, including gestational age at delivery and birth weights, were similar between the two groups: 44% of women were delivered by Cesarean and 59% received antenatal antibiotic. There were no differences in meconium stained fluid cases (16%) or Apgars <7 (13%). Among the HIV+ women, 52% were receiving HAART. There were no differences in maternal hematologic and iron indices except HIV+ mothers had a decreased WBC (8.7 vs. 9.9 X 1000/mm³ (P=0.043) and increased ferritin (69 vs 33ng/ml, P=0.029). CB ferritin was also significantly higher in the HIV+ group (231 vs 160ng/ml, P=0.029), but there was not a significant correlation between maternal and CB ferritin levels. CB ferritin correlated with other iron indices except sTfR. Inflammatory markers were not significantly different between the two groups and there was no relationship between ferritin and CRP and IL-6. There was, however, an inverse relationship between ferritin and sRAGE (r=-0.43, P=0.003) in the HIV+ group but not the HIV- group.

Conclusions This research demonstrated elevated ferritin levels among HIV-infected pregnant women, a finding that has previously been associated with a poorer prognosis in non-pregnant HIV+ individuals. Additionally, our study shows for the first time that ferritin is significantly elevated in cord blood of HEU infants. The finding that markers of inflammation (CRP, IL-6) were unchanged suggests that the increase in ferritin is unlikely caused by inflammation. We hypothesize that ferritin is produced in the placenta and that the inverse relationship between ferritin and sRAGE in CB suggests that oxidative stress may play a role in modulating ferritin levels. Further research is necessary to explain these findings and to determine whether this might contribute to adverse outcomes among HEU infants.

No conflict of interest

Abstract:P_76

Prevention of Mother-to-Child transmission

Extended prophylaxis with nevirapine for HIV-exposed infants: early outcomes in field conditions

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Background: Breastfeeding accounts for up to a third of vertical HIV transmission. However,
breastfeeding substantially reduces early childhood morbidity and mortality, particularly in resource-deprived settings where safe formula feeding is problematic. Research has identified effective prophylactic regimens for HIV-exposed breastfeeding infants. We examined outcomes in field conditions after implementing prophylaxis with extended nevirapine (NVP) for HIV-exposed infants in Kinshasa, Democratic Republic of Congo.

**Materials and Methods:** We analyzed routinely collected data on HIV-exposed infants enrolled into care and treatment who had a DNA PCR test between December 2009 and February 2012, and whose mothers reported exclusive breastfeeding. Infants without a DNA PCR result and those without a test before age 3 months were excluded. Logistic regression was used to generate crude and adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for the effect of receiving extended NVP on vertical transmission, defined as a positive result at the first DNA PCR test.

**Results:** Among the 472 infants included in the analysis, 313 (66%) received extended NVP prophylaxis. Overall, 33/472 (7%) had a positive DNA PCR, with a median age at testing of 7 weeks overall and for both exposure groups. Mothers with available data (N=450) received prophylaxis with single-dose NVP (18%), prophylaxis with AZT (33%), antiretroviral treatment (46%), or no PMTCT regimen (3%). Extended NVP reduced vertical transmission (crude OR: 0.35; 95% CI: 0.17, 0.71). Adjusted for infant single-dose NVP at birth, maternal CD4 count, and maternal PMTCT regimen, the OR was 0.29 (95% CI: 0.07, 1.18).

**Conclusions:** Extended prophylaxis with NVP can substantially decrease transmission in the first three months of life among HIV-exposed infants who exclusively breastfeed and receive care in field conditions. Prolonged breastfeeding coupled with extended NVP prophylaxis for HIV-exposed infants is feasible and effective in resource-deprived settings and should be further scaled-up.

*No conflict of interest*

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**Abstract: P_77**

**Prevention of Mother-to-Child transmission**

**Factors Associated With Dietary Quality Among HIV-Infected Women in the 3rd Trimester of Pregnancy**


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**Introduction:** Dietary factors in pregnancy are linked to complications of pregnancy and adverse perinatal outcomes. However, associations of dietary quality with demographic factors, food insecurity, nutrition support services, HIV disease severity and antiretroviral therapies have been poorly defined among HIV+ pregnant women. Our objectives are to assess dietary quality among participants in a multisite US cohort of HIV+ women in the 3rd trimester of pregnancy, and to examine correlates of dietary quality including demographic, socioeconomic, and HIV-disease specific factors.

**Material and Methods:** Among 225 HIV+ women enrolled in the NICHD-sponsored Pediatric HIV/AIDS Cohort Study (PHACS) Surveillance Monitoring for ART Toxicities (SMARTT) protocol, we assessed diet in the 3rd trimester of pregnancy with three 24-hour multiple-pass dietary recalls over a 2-week period. We did not include hospitalized women, women deemed unreliable during the interview, and multiple births. We centrally administered three 24-hour multiple-pass dietary recalls over a 2-week period and a food security questionnaire (USDA) by a telephone interview. We assessed diet quality with the Healthy Eating Index (HEI), which includes 12 components including foods and nutrients. We measured body mass index, HIV disease severity (CD4, viral load), and ARV exposures. Predictors of HEI were evaluated by classification and regression trees (CART), an interactive computer intensive technique which
seeks to identify sub-groups of individuals by maximizing differences in a dependent effect (i.e. HEI) over a collection of suspected correlates (independent variables).

Results: Mean age was 28y (range: 16-42), 75% were Black and 32% were born outside of the continental US; 33% had less than a 12th grade education and 12% used tobacco. The mean CD4 was 545 cell/mm³ (range: 7-1512), 81% had HIV viral load <400 copies/mL, and 95% were on HAART. The mean HEI score was 56.5 (range: 34-91 [0-100 scale]). Thirty-seven percent were food insecure, and 86% were enrolled in the Women, Infants and Children (WIC) program. In a multivariable analysis adjusted for mother's age, race, birthplace, education, drug exposure, tobacco use and receipt of WIC support, women born outside the continental US had higher HEI (63.6 vs 53.3, R²=17%). For those women born within the US, Black race was associated with a lower HEI (51.7 vs 59.5, R²=5%). For Black women born in the US, lower education and tobacco use in the 3rd trimester were associated with the lowest HEI (45.2). Women born outside the continental US, aged 29-40 had the highest HEI (68.3). Although HEI was higher among women receiving WIC support than not (57.1 vs 51.2; P=.01), it was not a factor in the final CART model. HIV-specific covariates or other drug exposures were not associated with HEI.

Conclusion: In this cohort of pregnant HIV+ women, dietary quality was relatively low, and food insecurity was common. Lower HEI score was associated with US birth, Black race, lower education, and tobacco use, but not with HIV-specific factors. Interventions to improve access to healthful food choices have the potential to improve pregnancy outcomes in HIV+ women, although further study is required.

No conflict of interest

Abstract: P_78

Prevention of Mother-to-Child transmission

Receipt of cART among childbearing women in Ukraine: implications for vertical and horizontal transmission

Introduction: Ukraine has the highest adult HIV prevalence in Europe estimated at 1.6%. At the end of 2007, combination antiretroviral therapy (cART) became available in Ukraine for women requiring it for PMTCT only (WHO 'Option B'), as well as for those requiring treatment for their own health.

Methods: Data on 3535 mother-child pairs enrolled in the Ukraine European Collaborative Study between January 2008 and December 2010 were analysed to assess coverage of antenatal cART, to investigate factors associated with its receipt and to assess the impact on MTCT. Data from a nested postnatal cohort of mothers were analysed to explore issues relating to onward HIV transmission.

Results: Overall, antenatal cART was received in 45% (n=1606) of pregnancies, increasing from 22% (270/1217) in 2008 to 55% (709/1291) in 2009 and 61% (627/1027) in 2010 (p<0.01). In the remaining pregnancies, ZDV monotherapy (ZDVm)+/- sdNVP predominated (n=1573). Where used, cART was usually started in pregnancy, with only 4% (n=131) of woman on cART at conception. At first antenatal measurement, 34% (774/2264) of women had a CD4 count ≤350 cells/mm³ and 14% were at WHO stage 3 or 4. Factors significantly associated with a lower likelihood of receipt of antenatal cART (versus ZDVm) in adjusted analyses included earlier calendar year, lower maternal educational level, WHO stage 1 or 2 (vs. stage 3 or 4) disease and centre. Antenatal CD4 counts pre-treatment were not available for all women; among those on cART with CD4 counts, 47% (519/1113) were receiving this for PMTCT only (CD4 count ≥350 and WHO stage 1 or 2). The overall unadjusted MTCT rate was 4.1% (95%CI 3.4-4.9); stratified by type of antiretroviral prophylaxis/treatment, rates were 1.3% (95%CI 0.7-2.0) among mother-infant pairs with antenatal cART (n=1274), 3.8% (95%CI 2.8-5.0) among those with ZDVm (n=1342), 18.6% (95%CI 12.3-26.4) among those with sdNVP.
only (n=129) and 22.9% (95% CI 15.4-32.0) among those with no ART (n=109). In multivariable analysis of MTCT risk, adjusting for preterm delivery, mode of delivery, infant sex, IDU history, year of delivery and centre, antenatal cART was associated with a 69% reduced MTCT risk versus ZDVm (adjusted odds ratio 0.31 95%CI 0.17-0.57, p<0.01). In a sub-group of 2377 women followed postnatally in a linked cohort, 24% (n=565) continued ART after delivery. Among untreated married/cohabiting women who had an HIV-negative partner (29%, 429/1488) or did not know their partner's HIV status (31%, n=459), 77% (684/888) reported using condoms. However, 27% (n=184) reported also using withdrawal for family planning (i.e. inconsistent condom use). Among all sexually active women, 25% of those on ART (104/423) and 26% of those untreated (324/1255) were using no contraception or withdrawal only.

Conclusions: In this lower middle-income setting, despite the adoption of an 'Option B' policy, 39% of women delivering in 2010 did not receive cART. In this relatively healthy population, most women do not require treatment postnatally. The scope for onward transmission to sexual partners is demonstrated by the one in three untreated women who are in discordant couples and their lack of or inconsistent condom use.

No conflict of interest

Abstract: P_79

Prevention of Mother-to-Child transmission

First trimester exposure to antiretroviral therapy and risk of birth defects among infants born to HIV-infected women on Tennessee Medicaid Program


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Background: The use of antiretroviral therapy (ART) during pregnancy is considered the standard of care for HIV-infected (HIV+) pregnant women. A few studies have indicated that use of some ARTs during pregnancy may be associated with an increased risk of birth defects, but the evidence remains inconclusive. Most ARTs are classified as FDA class B or C because of insufficient evidence, except for efavirenz, which is classified as class D based on animal studies and case reports. We evaluated the association between first trimester exposure to ARTs and birth defects in HIV+ women enrolled in Medicaid.

Methods: We linked data from Tennessee Medicaid files and vital records to identify infants born to HIV+ females delivering between 1994 and 2009. Maternal HIV status was defined based on diagnosis codes, prescriptions for ARTs, and codes for CD4 count or viral load procedures. ART exposure was identified from pharmacy claims. Birth defects were identified at any point during the infant's first year of life from maternal and infant diagnosis claims and vital records. Medical charts for all infants with birth defect claims were reviewed and only confirmed, major diagnosis were considered a case. Logistic regression models were used to evaluate associations between first trimester ART exposure and birth defects adjusting for maternal age and race.

Results: In total, 806 infants met our study inclusion criteria (including 20 sets of twins). 26 (3.2%) infants had at least 1 major birth defect, most (54%) in the cardiac system. Compared to infants without first trimester ART exposure, there was no increased risk for infants exposed in the first trimester to ART overall (OR = 1.13; 95% CI: 0.47 – 2.70) or to specific ARTs. Of the 21 infants exposed to efavirenz, none had a birth defect (0%; 95% CI: 0.0-13.2%). The prevalence of defects was higher among infants whose mothers had HIV-related illnesses during pregnancy (15% vs. 4%; p<0.0001).

Conclusions: In this Medicaid cohort of HIV+ women there was no increased risk of birth defects associated with first trimester ART exposure. We had limited power to study specific ARTs.

No conflict of interest
Abstract: P_80

Prevention of Mother-to-Child transmission

A survey of national guidelines for the prevention of mother-to-child transmission of HIV across Europe

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Background: Europe includes some countries that have achieved 'virtual elimination' of mother-to-child transmission (MTCT) of HIV, but others that have not, mainly in Eastern Europe. Although antenatal HIV screening policies have been serially assessed across Europe in the past, to date there has been no attempt to contrast and compare national PMTCT policies across Europe as a whole.

Materials and Methods: A survey was conducted using a structured questionnaire sent to experts in 21 European countries January to March 2012, requesting a copy of the national guidelines, if unpublished. Our aim was to ascertain, summarize and compare national PMTCT guidelines across Europe. Responses were received from 21 countries: Belgium, Denmark, Estonia, Finland, France, Germany/Austria (conjoint guidelines), Greece, Ireland, Italy, Lithuania, Moldova, Norway, Poland, Portugal, Russia, Spain, Sweden, Switzerland, The Netherlands, UK and Ukraine. No responses were received for Bulgaria, Czech Republic and Slovakia.

Results: In all 21 countries, there was a policy to recommend antenatal HIV screening for all pregnant women; in 13 (62%) there was an opt-out screening strategy and in 8, an opt-in policy. Sweden and Norway were the first to recommend universal screening (in 1987), with Denmark updating from a selective to a universal screening policy most recently (2010). For HIV-positive women in whom the only indication for ART was PMTCT, the recommended gestational age for commencing antenatal ART varied from 10 to 28 weeks: initiation of ART before 19 weeks gestation was recommended in guidelines from Denmark, Estonia, Finland, Greece, Italy, Norway, Poland, Portugal, Russia, Spain and Sweden; in the UK, France, Belgium and the Netherlands, there was a wide range, from 14-24 weeks, while the Swiss and Ukrainian guidelines recommended starting at 24-28 weeks and the German/Austrian and Lithuanian at 28 weeks. A minority of national guidelines recommended inclusion of zidovudine in antenatal cART regimens (n=6). In 9 guidelines it was recommended that zidovudine is used intrapartum for all infected women, with the remainder recommending its use in specific situations, including lack of antenatal ART, detectable viral load at delivery and preterm delivery. In most (n=20) countries surveyed, national guidelines recommended that a group of HIV-positive women (usually those on successful cART) can have a vaginal delivery. Viral load thresholds for vaginal delivery were <1000 copies/ml in 5 countries, <400 copies/ml in 3, <200 copies/ml in 1 and <50 copies/ml in 11 countries. Most guidelines recommended that mode of delivery decisions should be based on viral load measurement at 36 weeks (n=12); in Italy, decision-making was recommended at 30-34 weeks, while in the Netherlands, women with detectable HIV viral load at 36 weeks can be considered for a vaginal delivery if they achieve <50 copies/ml at term. In 10 countries, 4 weeks zidovudine monotherapy for neonatal prophylaxis was recommended, with 1 week recommended in Ukraine; in the Netherlands, the recommendation was for 4 weeks of ZDV/3TC prophylaxis.

Conclusion: There are some important differences across Europe in national PMTCT guidelines, with most variation seen for issues where the evidence-base remains limited.

No conflict of interest
Abstract: P_81

Prevention of Mother-to-Child transmission

Characterization of memory T cells and CCR5 expression in HIV-1-infected human cord blood

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Introduction

Previous work with SIV in rhesus macaques has found that low levels of CCR5 expression in CD4+ central memory cells is protective against progression towards AIDS. Little work has been done characterizing CCR5 expression in memory T cell populations in cord blood, as a potential correlate of protection during on-going HIV-1 exposure. Here we determined the proportions of effector and central memory T cells and expression of CCR5 in human cord blood in the absence and presence of HIV-1.

Materials & Methods

Cord blood mononuclear cells (CBMCs) were stimulated with PHA and IL-2 for three days prior to 24-hour HIV-1<sub>Bal</sub> infection or left unstimulated. Cells were stained with conjugated antibodies, and fixed and analyzed by flow cytometry.

Results

Unstimulated HIV-1-infected CD4+ (SP) and CD4+CD8+ (DP) T cells expressed higher levels of the central memory phenotype (CD95+CCR7+), while stimulated HIV-1-infected SP and DP T cells expressed higher levels of the effector memory phenotype (CD95+CCR7-). The proportions of DP T cells increased in unstimulated HIV-1-infected samples (8-14%), compared to uninfected samples (<1%). In both memory subtypes of unstimulated HIV-1-infected T cells, there were low levels of CCR5 expression in SP cells (2-3%) and moderate CCR5 expression in DP cells (52-68%). Stimulated HIV-1-infected memory cells had moderate levels of CCR5 expression in SP (16-28%) and DP (33-34%) T cells. Only in stimulated central memory cells did we note low rates of HIV-1 infectivity and CCR5 expression in SP (15%) and DP (4%) T cells. Stimulated effector memory T cells and both memory subtypes of unstimulated T cells had low rates of HIV-1 infectivity (0-2%). Though DP memory T cells expressed greater proportions of CCR5 they showed lower rates of HIV-1 infectivity, compared to SP memory T cells.

Conclusions

Low levels of CCR5 expression in cord blood CD4+ memory T cell populations are associated with low rates of HIV-1 infectivity. This data may explain why vertical transmission of HIV-1 occurs relatively infrequently in HIV-1-exposed infants even in the absence of recommended medical interventions.

No conflict of interest

Abstract: P_82

Prevention of Mother-to-Child transmission

Antiretroviral drug resistance profile in a cohort of HIV-infected pregnant women in a center of PMTCT in Rio de Janeiro

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Background:

Antiretroviral (ARV) use in pregnancy is the cornerstone to reduce the rate of mother-to-child-transmission (MTCT) of HIV. There are few data addressing the resistance to ARV drugs during the pregnancy in Brazil. The knowledge of HIV resistance mutations associated with antiretroviral resistance in pregnant women is important to guide antiretroviral use during pregnancy and to select future ARV treatment options for the mothers and their infected infant.

Methods:

Genotyping test data were collected retrospectively by chart review of HIV-infected pregnant women in a prenatal care clinic. To perform the genotyping test the criteria is a viral
load (VL) > 2000 copies/mL at the entry in the cohort. The TRUGENE platform was used. ARV mutations genes were analyzed using Stanford Database. Statistical analysis was performed using SPSS version 17.0.

**Results:** From April 2010 to October 2011, 240 charts were reviewed. One hundred forty two pregnant women were included and met the criteria for genotyping. One hundred and thirty were tested for genotyping. Of the 157 ARV naïve subjects, 91(58%) were genotyped and 9/91(10%) had a gene mutation. Seventy five pregnant women had prior ARV for PMTCT or were using ARV for treatment; from these, 34(45%) were genotyped and 12/34 (35%) had a gene mutation. Among these 34 ARV-experienced women, 15/34(44%) used ARV for PMTCT and 19/34(56%), for treatment. Five women were genotyped and no information on the use of ARV (one gene mutation) was found.

**Conclusion:** Resistance to ARV was higher in antiretroviral-experienced pregnant women (35%) than in ARV naïve women (10%). In both groups, NNRTI resistance was very high (92 and 78%). Survey of ARV resistance by genotyping test is an important tool to choose the ARV regimen.

*No conflict of interest*

**Abstract: P_83**

*Prevention of Mother-to-Child transmission*

**HIV-negative babies born to HIV-positive mothers have weakened ability to fight some infections**

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**Introduction:** Babies who are exposed to HIV at birth but don't become infected with the virus have lower levels of antibodies to diseases such as whooping cough, tetanus and pneumococcus. The findings might explain in part why uninfected babies born to women with HIV have a higher risk of illness and death early in life in Mbingo Baptist Hospital (June – Dec. 2011).

**Materials and Methods:** Randomised Clinical Trial study whereby, antibody levels of 109 HIV-positive and HIV-negative pregnant women were measured before birth, and the antibody levels of their infants measured after birth, according to the release. The researcher also assessed how the babies responded to routine vaccination by measuring the babies’ antibody levels at four months, after they had received their routine vaccines.

**Results:** Before the infants were vaccinated, the research shows that, of all infants exposed to HIV before birth without becoming infected themselves, 17% had antibody levels thought to protect against HiB, or HiB, compared with 52% of infants without exposure; 21% of those exposed had antibodies against hepatitis B compared with 54% of unexposed babies. HIV-positive mothers had lower levels of antibodies to HiB and pneumococcus, and not to whooping cough or tetanus, the researchers found. HiB can cause meningitis and pneumonia. After being vaccinated, the researcher found that HIV-exposed uninfected infants compared with HIV-unexposed infants had robust antibody responses following vaccination, with higher antibody responses to pertussis and pneumococcus. 'Once the HIV-exposed, uninfected babies received their routine vaccinations, they had antibody levels similar to, or higher than, HIV unexposed infants, meaning that they were likely to be well protected by vaccination. The researcher added that more research is needed to establish whether babies exposed prenatally to HIV could be better protected against infections through earlier vaccination, or through vaccine shots given to mothers before the children are born. He concluded that targeted vaccination strategies may be required in HIV-infected women and their infants.

**Conclusions:** The findings might mean a lot to the growing number of HIV-exposed infants worldwide. While births of HIV-positive babies have dropped dramatically in the past decade due to medications that mothers can take during pregnancy to prevent transmission, infectious disease remains a major killer of children under five, killing close to six million children globally each year.
Abstract: P_84

Prevention of Mother-to-Child transmission

Child Health Outcomes in Blantyre, Malawi: 20-Years of Data from Multiple Longitudinal HIV Cohorts

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Background: Longitudinal data from established research sites provide a unique opportunity to examine trends. In this analysis, data collected over a period of 20 years (1989-2009) from multiple prospective cohort studies at a single research site in Blantyre, Malawi were examined for trends and risk factors for three key child health outcomes: birth weight (BW), gestational age (GA), and child mortality.

Methods: Data from six cohorts were analyzed for mean BW and GA. Frequencies of low birth weight (LBW; <2500g), preterm (PT) birth (GA<37 weeks), and child mortality (five cohorts) were stratified by HIV status of the mother and child. Children born to HIV-infected mothers (and to uninfected mothers for mortality outcomes) were followed for up to two years from birth. In all studies, women were recruited from the antenatal clinic at the main hospital in Blantyre and from 5 health centers covering the hospital catchment area. Two studies were observational cohorts to determine rates and risk factors for mother-to-child transmission (MTCT) of HIV. Four studies were phase 3 clinical trials to decrease the rate of HIV MTCT using antiretroviral (ARV) and non-ARV interventions. Most studies predated the use of combination ARV therapy (ART) during pregnancy. We assessed risk factors for LBW and PT birth using mixed-effects logistic regression. Mortality rates were estimated using birth-cohort analysis. Multivariable Cox regression models were used to identify risk factors for mortality. We present adjusted odds ratios (aOR) and hazard ratios (aHR). Human subjects approval and informed consent were obtained in all studies.

Results: Between 8286 and 8874 infants were included in each model, depending on the specific analysis. Mean BW ranged from 2793 to 3079 g and mean GA from 37.8 to 39.0 weeks. Greater maternal age and higher maternal education level were associated with significantly (p<0.05) lower odds of LBW (aOR 0.98 and 0.67, respectively) and PT birth (aOR 0.97 and 0.70, respectively). Female infant gender increased the odds of both LBW and PT birth. Mortality rates (per 100 person-years) were 3.1-6.9 among all infants born to HIV-uninfected mothers. Among uninfected infants born to HIV-infected mothers, mortality rates were 2.5-7.5. For all children born to HIV-infected mothers, the rates were 11.4-17.2, while for children who themselves became HIV-infected, the rates were 15.6-57.4. Only greater BW (per 100 grams) was consistently and significantly associated with lower child mortality (aHR range 0.89-0.96).

Conclusions: No substantial changes in BW, GA and child mortality levels were observed over time. HIV continues to contribute to high levels of child morbidity and mortality in the African setting. Continuous evaluation of these outcomes and modifiable risk factors is needed in Blantyre, Malawi where 20% of reproductive-age women are HIV-infected. With expanding access to ART, these data from the pre-treatment era will be valuable for evaluating long-term trends and determining the population-level impact of future interventions.

No conflict of interest

Abstract: P_85

Prevention of Mother-to-Child transmission

Is exclusive breastfeeding for HIV positive mothers only

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Abstract: P_86

Prevention of Mother-to-Child transmission

Exclusive Breastfeeding and Postnatal HIV Transmission among HIV-1 Infected Women and their Infants: Findings from a cohort study in Kampala, Uganda

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Introduction: World Health Organization (WHO) Infant Feeding recommendations for HIV-infected women and their exposed infants in resource-poor nations have been evolving, and currently promote 6 months exclusive...
breastfeeding (EBF) for the majority of HIV infected women in resource limited settings. However, adherence to these guidelines supporting 6 months EBF is challenging due to local cultural norms and varies by population. In this analysis we evaluated the frequency of infant feeding practices and postnatal HIV transmission among breastfeeding HIV exposed infants enrolled in an ongoing observational breastfeeding cohort study in Kampala, Uganda.

Materials & Methods: From March 2010 to May 2011, HIV seropositive pregnant women who presented for antenatal care were recruited from the Mulago National Referral Hospital PMTCT program. Women who chose to breastfeed their infants were offered study participation if they met other eligibility criteria. These women received antiretroviral (ARV) prophylaxis given antenatally and intrapartum followed by nevirapine prophylaxis to the infants. HIV-infected women were provided infant feeding counseling consistent with the WHO/Uganda Ministry of Health guidelines prior to recruitment and at every scheduled study visit.

Results: 100 HIV-infected women with >350 CD4+ T cells/µL and their infants were enrolled and followed up at 2, 6, 12, 18, 24, 36 and 48 weeks post partum. The proportion of women practicing EBF was 100% at birth, and 90.63% (87/96) among those who completed 12 weeks of follow-up. By 24 weeks (6 months) the proportion of women practicing EBF was 63.54% (61/96). Among the participants who had completed 36 weeks (9 months) of follow-up there were 3 women who continued to practice EBF. The percentage of women practicing mixed feeding prior to 6 months was low and increased from about 1.02% (1/98) at 2 weeks to about 8.33% (8/96) at 24 weeks. The proportion of women who reported practicing replacement feeding prior to 6 months was also low but rose with increase in age of the infants from about 1.02% (1/98) at 2 weeks to 28.13% (27/96) at 24 weeks. The median age of exclusive breastfeeding cessation was at 24.6 weeks (interquartile range 18.4 to 27 weeks). Only one infant was found to be HIV-infected at birth with no new postnatal infections among 92 infants and 74 infants who completed 36 weeks (9 months) and 48 weeks (12 months) of follow-up respectively.

Conclusions: Interventions supporting 6 months of EBF and ARV prophylaxis allowing longer and safer duration of breastfeeding were associated with increased rates of exclusive breastfeeding and low rates of postnatal HIV transmission. These results underscore the need to strengthen counseling messages to support 6 months exclusive breastfeeding which, when coupled with ARV prophylaxis, helps reduce the risk of postnatal transmission while avoiding the social stigma, morbidity and mortality associated with early cessation or non-breastfeeding.

No conflict of interest

Abstract: P_87

Implementation research on PMTCT and pediatric treatment programs

Towards elimination of mother-to-child transmission of HIV: the impact of a rapid results initiative in Nyanza Province, Kenya

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Background: Despite extensive scale-up of Prevention of Mother-to-Child Transmission (PMTCT) services in Kenya, many HIV-infected women and exposed infants do not access comprehensive preventive services. Novel approaches are needed to improve PMTCT provision.

Objective: To assess the effect of a PMTCT Rapid Results Initiative (RRI) on PMTCT service provision.

Methods: A RRI was designed and implemented by Family AIDS Care and Education Services (FACES) and the Kenyan Ministries of Health to address key challenges including CD4 testing, highly active antiretroviral therapy (HAART) initiation for pregnant women and infants, male involvement, and Early Infant
Diagnosis (EID). The RRI was carried out over a 12 week period at 119 health facilities in Nyanza Province. Strategies encompassed accelerated community mobilization, strengthened laboratory networking, and health workforce support. We computed risk ratios (RR) and 95% Confidence Intervals (CI) using pre-post cohort analysis to compare site-level data for each indicator during and post-RRI to site-level baseline data.

**Findings:** CD4 uptake among HIV-infected pregnant women increased by 13% (RR=1.1, 95% CI=1.1-1.2) during RRI and remained elevated post-RRI (RR=1.1, 95% CI=1.0-1.1) compared to baseline. The relative proportion of HAART initiation improved from 13.7% to 19.7% among pregnant HIV-infected women (RR=1.4, 95% CI=1.2-1.7) during the RRI and to 21.7% (RR=1.6, 95% CI=1.4-1.8) post-RRI. Uptake of EID among exposed infants increased by 30% during RRI (RR=1.3, 95% CI=1.2-1.4) and by 90% post-RRI (RR=1.9, 95% CI=1.8-2.0). Infants initiated on HAART increased from 54.8% to 60.1% (RR=1.1, 95% CI=0.9-1.4) during RRI and to 69.0% post-RRI (RR=1.3, 95% CI=1.0-1.6). Male partner testing increased from 7.7% at baseline to 16.4% during the RRI (RR=2.1, 95% CI=2.0-2.3).

**Conclusion:** Significant and sustained improvement in PMTCT services and outcomes can be achieved using an RRI intervention. Similar strategies should be employed country-wide to eliminate vertical transmission.

No conflict of interest

**Abstract: P_88**

*Implementation research on PMTCT and pediatric treatment programs*

**Low rates of early mother-to-child HIV transmission in a routine programmatic setting in Lilongwe, Malawi**

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**Introduction:** Data on PMTCT effectiveness within routine healthcare delivery in resource-constrained settings is limited. We sought to evaluate the impact of PMTCT delivery and maternal CD4 count on early HIV transmission within the Tingathe program in Lilongwe, Malawi. Tingathe utilizes community health workers to ensure mother-infant pairs receive all PMTCT services.

**Methods:** We reviewed clinical records of all 1088 mother-infant pairs enrolled March 2009-March 2011 who completed follow up to first DNA PCR. The CD4 cutoff for ART eligibility changed from 250 to 350 in August 2010. Women on ART at enrollment did not receive CD4 testing. The recommended PMTCT regimen for women ineligible for ART was complete combination prophylaxis—mother: AZT for at least 6 weeks+sdNVP+combivir tail, and infant: sdNVP+AZT. Incomplete combination prophylaxis was defined as non-completion of any component of complete combination prophylaxis. Early ART was defined as ART for >14 weeks prior to delivery. We determined transmission rates with confidence intervals and compared these rates using global chi-square tests, followed by post-hoc pairwise testing to evaluate differences between multiple proportions.

**Results:** Table 1 presents HIV transmission rates at first PCR stratified by PMTCT regimen. Overall MTCT rate at first PCR was 4.1%. Early ART was associated with reduced transmission, compared to all other treatment groups (p < 0.005).

Table 2 presents transmission results for mothers not on ART at enrollment stratified by CD4 count. No difference in early transmission was detected between various CD4 levels (p = 0.308).

**Conclusion:** Low rates of early MTCT of HIV are possible in resource-constrained settings under routine programmatic conditions. Early ART is more protective than any other regimen.
Furthermore, in the context of timely initiation of ART and PMTCT prophylaxis, baseline CD4 does not impact transmission among women not on ART at baseline. Efforts to improve timely initiation of ART and PMTCT prophylaxis are needed.

No conflict of interest

Table 1: Early Transmission Rates by PMTCT medication regimen

<table>
<thead>
<tr>
<th>Mother PMTCT Medication</th>
<th>Infant PMTCT Medication</th>
<th>Total PCR results available, n=1088</th>
<th>First PCR negative, n=1043</th>
<th>First PCR positive: infected, n=45</th>
<th>Early MTCT Rate*</th>
</tr>
</thead>
<tbody>
<tr>
<td>None/Unknown/sd-NVP</td>
<td>None/Unknown or sdNVP</td>
<td>59</td>
<td>52</td>
<td>7</td>
<td>11.9 (5.6 – 22.8)%</td>
</tr>
<tr>
<td>Incomplete combination prophylaxis</td>
<td>sdNVP+AZT or sdNVP+AZT+ CBV tail</td>
<td>73</td>
<td>66</td>
<td>7</td>
<td>9.6 (4.5 – 18.8)%</td>
</tr>
<tr>
<td>Complete combination prophylaxis</td>
<td>sdNVP+AZT+ CBV tail</td>
<td>472</td>
<td>448</td>
<td>24</td>
<td>5.1 (3.4 – 7.5)%</td>
</tr>
<tr>
<td>LATE ART: ART &lt;14 weeks before delivery</td>
<td>ART</td>
<td>187</td>
<td>180</td>
<td>7</td>
<td>3.7 (1.7 – 7.7)%</td>
</tr>
<tr>
<td>EARLY ART: ART ≥14 weeks before delivery</td>
<td>ART</td>
<td>297</td>
<td>297</td>
<td>0</td>
<td>0.0 (0.0 – 1.5)%</td>
</tr>
</tbody>
</table>

*Early MTCT rate calculation: number infected/number of PCR results available

Table 2: Early Transmission Rates By Maternal CD4 count for women not on ART at program enrollment

<table>
<thead>
<tr>
<th>CD4 cells/mm³</th>
<th>Total PCR results available, n=804</th>
<th>First PCR negative, n=767</th>
<th>First PCR positive: infected, n=37</th>
<th>Early MTCT Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-99, n</td>
<td>35</td>
<td>34</td>
<td>1</td>
<td>2.9 (&lt;0.01 – 15.8)%</td>
</tr>
<tr>
<td>100-199, n</td>
<td>100</td>
<td>97</td>
<td>3</td>
<td>3.0 (0.7 – 8.8)%</td>
</tr>
<tr>
<td>200-349, n</td>
<td>206</td>
<td>192</td>
<td>14</td>
<td>6.8 (4.0 – 11.1)%</td>
</tr>
<tr>
<td>350-499, n</td>
<td>225</td>
<td>213</td>
<td>12</td>
<td>5.3 (3.0 – 9.2)%</td>
</tr>
<tr>
<td>≥500, n</td>
<td>238</td>
<td>231</td>
<td>7</td>
<td>2.9 (1.3 – 6.1)%</td>
</tr>
</tbody>
</table>

*1088 available PCR results, of these 261 mothers were already on ART, 23 with no corresponding maternal CD4 results, therefore 804 available CD4 results with corresponding PCR results.
Abstract: P_89

Implementation research on PMTCT and pediatric treatment programs

Comparison of HIV-Genotyping Results Obtained from Next-generation Sequencing of Plasma and Dried Blood Spot Samples

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Introduction. There is emerging evidence that the presence of low-frequency HIV variants with drug resistance may influence response to antiretroviral treatment. HIV genotyping using next generation sequencing (NGS) may offer an advantage over standard population genotyping (SPG) that is currently the gold standard in the field. Barcoding of samples from individual patients allows multiple samples to be run in parallel, lowering the cost of NGS. Adaptation of NGS methods for HIV genotyping using dried blood spot (DBS) samples could facilitate use of this approach in resource-limited settings. We assessed concordance between results obtained using NGS to analyze plasma and DBS samples; this analysis included detection of antiretroviral drug resistance mutations (DRM) and determination of the frequency of mutations in the viral population in each sample.

Material & Methods. Blood samples were collected from 49 HIV-infected, African children enrolled in the P1060 clinical trial who were previously exposed to single dose nevirapine. The samples were collected prior to antiretroviral treatment initiation. A single blood sample was used to prepare plasma and DBS samples. Total nucleic acid was extracted from five spots on each DBS card (equivalent to 250 uL of blood). Extracted nucleic acid was subjected to reverse transcription (to generate cDNA from HIV RNA) followed by a single-round of amplification with barcoded primers (five unique identifiers) for four overlapping regions (amino acid positions: 8-260 in HIV reverse transcriptase [RT]). Five barcoded samples were pooled in a single picotitre lane and sequenced from an 8-lane plate (Roche 454 GS FLX Sequencing Platform).

Results. For 33 (67.3%) of the 49 DBS samples, sufficient sequence data was obtained to analyze HIV RT. Analysis was successful in 25/33 (75.8%) of samples that had been stored correctly compared to only 9/16 (56.3%) of samples with sub-optimal storage (p=0.198). DRMs were detected in 27 matched DBS and plasma samples over a dynamic range of frequencies (1-100% mutant in the viral population, median: 3.4% (IQR 1.6-30.0%) vs. 3.5% (IQR 1.4-38.3%), respectively). There was 97.1% concordance between detection of DRMs in plasma and DBS samples. Discordance in DRM detection, which was observed in 14 samples, was more likely to occur when DRMs were present at low frequencies (median: 1.5%; IQR 1.2-3.2). Discordance was diminished to 1 sample if a threshold frequency of 5% DRM was used.

Conclusions. The overall success of genotyping using NGS was similar for properly-stored DBS samples (75.8%) and plasma samples (81.3%). While variants present at <5% may contribute to discordance in genotypes obtained with DBS and plasma samples, NGS can be used to detect and quantify DRMs present over a dynamic range (1-100%) of mutant frequencies. Where feasible, NGS may used for in-depth monitoring of HIV drug resistance, using plasma or DBS samples.

No conflict of interest

Abstract: P_90

Implementation research on PMTCT and pediatric treatment programs

Turnaround times for early infant diagnosis of HIV infection in rural southern Zambia

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Abstracts

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Background: Early infant diagnosis of HIV infection is challenging in sub-Saharan Africa, particularly in rural areas where the laboratory capacity and technology are unavailable. Specimens must be transported to central laboratories for testing, leading to delays in diagnosis and initiation of antiretroviral therapy. This study was undertaken in rural southern Zambia to measure the turnaround time for confirmation of HIV infection and identify delays in diagnosis.

Methods: Chart reviews were conducted between August 2010 and May 2011 for children undergoing early infant diagnosis at the HIV clinic in Macha, Southern Province, Zambia. Information on relevant dates, receipt of drugs by the mother or child to prevent HIV transmission (PMTCT), and test results was Abstracted.

Results: Between August 2010 and May 2011, 123 infants (54% male) had samples collected for early infant diagnosis at a median age of 1.6 (IQR: 1.4, 5.3) months. 82% of mothers and 76% of infants received PMTCT (53% of mothers received HAART and 50% of infants received single dose nevirapine plus seven days of AZT). The median time between specimen collection and arrival at the central laboratory in Lusaka was 13 days (IQR: 8, 18). The median time from arrival at the central laboratory to testing was 5 (IQR: 3, 5) days. The median time from arrival at the central laboratory to return of results to the clinic was 23 days (IQR: 9, 35). The median time from arrival of the results at the clinic to return of results to the caregiver was 46 days (IQR: 26, 67), resulting in a total median time from specimen collection to return of results to the caregiver of 84 days (IQR: 82, 92). 7% of test results were positive (2% among infants born to mothers who received PMTCT and 32% among infants born to mothers who did not), with a shorter total median time for infected infants (56 vs. 84 days; p=0.0002).

Conclusions: The longest delay in diagnosis was in the time required to provide results to caregivers. As the time for transport and testing was variable and caregivers had to travel long distances to get to the clinic, clinic appointments were scheduled at three month intervals. A more efficient process is needed so that caregivers can be provided test results more rapidly, potentially resulting in earlier treatment initiation and better outcomes for HIV-infected infants.

No conflict of interest

Abstract: P_91

Implementation research on PMTCT and pediatric treatment programs

Association between nevirapine-resistant HIV-variants and antiretroviral treatment outcomes in single-dose nevirapine exposed infants

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Introduction. Women and infants who received single-dose nevirapine (sdNVP) are at increased risk of virologic failure or death (VF/death) with NVP-based antiretroviral treatment (ART). We examined the association between NVP resistance mutations and time to VF/death in sdNVP-exposed infants in the IMPAACT P1060 trial (n=164).

Material & Methods. Next generation sequencing (NGS) was used to quantify NVP resistant HIV variants (≥1%) in 118 of 152 children whose samples were previously analyzed by population sequencing (7 missing samples, 27 not evaluable). Association of NVP resistance mutations with time to VF/death was examined in children randomized to NVP-ART (n=63) using Cox proportional hazards models.

Results: At study entry, 56% of the infants were <9 months of age, 98% had subtype C HIV, and 84% were not breast-fed. NVP resistance mutations were more frequently detected by
NGS than population sequencing (Table), with Y181C the most common. Detection of either Y181C or K103N by NGS decreased with age (p=0.01). Children with NVP resistance also detected by population sequencing had shorter time to VF/death (4 of 6) than children with no NVP resistance (14 of 51) [hazard ratio (HR) =3.8, 95% confidence interval (CI): 1.1-13.3, p=0.037]. However, no significant difference in VF/death was observed for children with NVP resistance detected only by NGS (3 of 6) [HR=1.5, 95% CI: 0.4-5.5, p=0.56] relative to children with no NVP resistance.

**Conclusions:** In contrast to adults, only high frequency baseline NVP resistance also detected by population genotyping was significantly associated with shorter time to VF/death in sdNVP exposed infants. Low-frequency baseline NVP resistance provided no additional predictive power (although sample size was limited). This suggests additional factors are contributing to NVP-based ART failure in children.

_No conflict of interest_

**Abstract: P_92**

*Implementation research on PMTCT and pediatric treatment programs*

**Addressing the quality gap in PMTCT services in low-resource settings: an evaluation of PMTCT 'Nurse Quality Mentors' in three South African provinces**

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**Introduction:** Most pregnant women living with HIV access government antenatal services, however, few receive the complete package of prevention of mother-to-child transmission (PMTCT) interventions in low-income settings. We evaluated whether clinical mentorship provided by nurse Quality Mentors (QMs) was effective in improving outcomes in the continuum of care of PMTCT services in South Africa.

**Materials & Methods:** QMs support PMTCT nurses working in rural and peri-urban primary healthcare clinics (PHCs). QMs strengthen staff capacity through ongoing mentoring and supervision, and ensure proper application of national PMTCT guidelines. An observational before-after study was conducted at 31 facilities in five high HIV prevalence districts (antenatal HIV prevalence 30% - 46%). Routine data collected between April 2010 and September 2011 was analysed, and PMTCT indicators were compared for the periods before and after QMs were introduced at each facility.

**Results:** A total of 4951 (pre) and 22,507 (post) women were included in analyses. Repeat HIV testing at 32 weeks gestation increased from 38% to 45% (RR=1.17; 95% CI: 1.12-1.23). Uptake of CD4 cell testing at booking increased from 82% to 85% (RR=1.03; CI: 1.01-1.05), and uptake of AZT for eligible women improved from 80% to 89% (RR=1.10; CI: 1.08-1.13) after introduction of QMs. HIV-exposed infants receiving cotrimoxazole around 6 weeks increased from 93% to 99% (RR=1.07; CI: 1.05-1.09). The proportion of infants HIV tested at 6 weeks and 18 months after birth increased from 69% to 77% (RR=1.07; CI: 1.08-1.16) and from 12% to 23% (RR=1.84; CI: 1.63-2.08), respectively, HIV transmission at 6 weeks and 18 months decreased from 3.3% to 2.7% (RR=0.80; CI: 0.58-1.10) and from 8.3% to 3.9% (RR=0.47; CI: 0.30-0.74), respectively.

**Conclusions:** QMs improved PMTCT cascade processes contributing to decreased HIV transmission. This is an effective strategy for health system strengthening in settings with limited human resources.

_No conflict of interest_
Abstract: P_93

Implementation research on PMTCT and pediatric treatment programs

Effect of implementing the WHO PMTCT guidelines (2010) on nutrition outcomes of HIV-exposed infants at Mulago National Hospital, Uganda

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Introduction: In 2010, Uganda started implementing the revised 2010 World Health Organization (WHO) Prevention of Mother to Child Transmission of HIV (PMTCT) guidelines strongly recommending that HIV exposed infants are breastfed for the first twelve months of life while receiving ARVs. This study establishes the effect of implementing the WHO 2010 PMTCT guidelines on nutrition outcomes of HIV exposed infants at Mulago National Hospital.

Materials and Methods: Clinical charts were reviewed for all HIV exposed infants aged 0-12 months who received PMTCT services between January, 2010 and December, 2011 at Baylor-Uganda supported postnatal clinic at Mulago National Referral Hospital. Data on age, infant feeding option and anthropometric measurements was extracted from the charts with complete records. Anthropometric measurements were analyzed in WHO Anthro software for classification of nutrition status (outcomes). Infants with weight-for-length, weight-for-age and length-for-age indices < -2 Z scores were respectively classified as wasted, underweight and stunted. Chi-square tests were used to compare the proportions of malnourished infants under the 2006 and 2010 guidelines using STATA 12.0 software.

Results: A total of 4,837 infants were included in the analysis: 33.8% under the 2010 guidelines. The proportion of exclusively breastfeeding infants < 6 months was 69.5% and 76.8% (p=0.06) respectively under the 2006 and 2010 guidelines. Among infants 6-12 months, 83.2% and 65.8% (p<0.001) had stopped breastfeeding under the 2006 and 2010 guidelines respectively. Seven percent (6.9%) compared to 13.1% (p<0.001) of infants 0-12 months were overweight, 1.9% (30/1600) compared to 1.2% (38/3148, p=0.05) were wasted while 16% compared to 30% (p<0.001) were stunted under the 2006 and 2010 guidelines respectively. Infants on WHO 2010 guidelines were 1.9X less likely to be wasted compared to infants on 2006 guidelines (OR: p=0.015). However, the infants on 2010 guidelines were 2X more likely to be stunted or underweight (p<0.001).

Conclusion: Wasting reduced among infants on WHO 2010 guidelines in line with the increased in prevalence of breastfeeding among HIV-exposed infants. However, the rates of chronic malnutrition increased among infants on WHO 2010 guidelines. Therefore, we recommend prospective studies to identify the underlying causes of increased chronic malnutrition among HIV exposed infants to guide implementation of the 2010 guidelines.

No conflict of interest

Abstract: P_94

Implementation research on PMTCT and pediatric treatment programs

Trends in antiretroviral usage and costs in a Thai pediatric HIV cohort: at 5 years of follow up.


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Results: A total of 4,837 infants were included in the analysis: 33.8% under the 2010 guidelines. The median age of infants was 6 months. The proportion of exclusively breastfeeding infants < 6 months was 69.5% and 76.8% (p=0.06) respectively under the 2006 and 2010 guidelines. Among infants 6-12 months, 83.2% and 65.8% (p<0.001) had stopped breastfeeding under the 2006 and 2010 guidelines respectively. Seven percent (6.9%) compared to 13.1% (p<0.001) of infants 0-12 months were overweight, 1.9% (30/1600) compared to 1.2% (38/3148, p=0.05) were wasted while 16% compared to 30% (p<0.001) were stunted under the 2006 and 2010 guidelines respectively. Infants on WHO 2010 guidelines were 1.9X less likely to be wasted compared to infants on 2006 guidelines (OR: p=0.015). However, the infants on 2010 guidelines were 2X more likely to be stunted or underweight (p<0.001).
Abstract: P_95

Implementation research on PMTCT and pediatric treatment programs

Prenatal syphilis and HIV transmission in Latin America and the Caribbean (LAC): achieving Pan-American Health Organization (PAHO) elimination goals


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Introduction: An estimated 459,000 children are born with congenital syphilis (CS) and 9,200 with HIV annually in LAC. PAHO has called for the elimination of CS and pediatric HIV by 2015. We used a validated simulation model of mother-to-child transmission (MTCT) of syphilis and HIV to project the impact of scaling up syphilis and HIV services in antenatal care (ANC) in LAC.

Materials & Methods: Using published data from LAC, we simulated a cohort of pregnant women, with syphilis prevalence of 1% and HIV prevalence of 0.5% (36% with CD4 ≤350/µL). We sought to identify conditions that would permit 'elimination,' defined by PAHO as <0.5 CS cases/1000 live births (LB), <0.3 infant HIV infections/1000LB, and HIV MTCT risk<2%. Base-case data inputs included: sensitivity of syphilis test: 83%, syphilis MTCT risk without penicillin: 37-94% (depending on maternal syphilis stage); syphilis MTCT risk with penicillin/maternal cure: 3%; HIV MTCT risk without antiretroviral drugs (ARVs): 17-27% (depending on maternal CD4); HIV MTCT risk with triple ARVs: 1-3%; and probability of intrauterine fetal demise (IUFD): 2-27% (depending on maternal disease and treatment).

We investigated two scenarios of access to care: 1) Current access (61% of women in ANC undergo syphilis and HIV testing, 65% receive penicillin if syphilis is identified, and 61% receive ARVs if HIV is identified), and 2) Ideal access (95% of women undergo testing, 95% receive penicillin if syphilis is identified, and 95% receive ARVs if HIV is identified). We conducted sensitivity analyses on all model input parameters, including: prevalence of syphilis (0-4%) and HIV (0-2.5%), syphilis test sensitivity (83-99%), lowest published HIV MTCT risks (13-20% without ARVs, 0.4-1.1% with ARVs), and lowest published syphilis MTCT risks (1% with maternal cure).

Results: In the current access analysis, we project 2.8 CS cases/1000LB, 0.7 HIV infections/1000LB, HIV MTCT risk of 13.7%, and 22.9 IUFD/1000 pregnancies. With ideal access, projected outcomes are decreased to 1.2 CS cases/1000LB, 0.2 HIV infections/1000LB (meeting a PAHO goal), HIV MTCT risk of 4.3%, and 22.3 IUFD/1000 pregnancies. To meet the PAHO CS elimination goal of <0.3/1000LB with ideal access, the prevalence of syphilis must be <0.4%. Improving syphilis test sensitivity to 99%, while also reducing syphilis MTCT after maternal cure to 1%, would reach the PAHO CS elimination goal at syphilis prevalences up to 0.8%. The PAHO goal of HIV MTCT <2% is only met under the ideal access scenario if the lowest published HIV MTCT risks are also assumed.

Conclusions: Increasing antenatal testing and treatment will substantially decrease MTCT of both CS and HIV in LAC, and will partially meet PAHO elimination goals for HIV. However, this strategy will not meet CS elimination goals at currently reported syphilis prevalences in LAC, nor will it meet HIV MTCT goals at average ARV efficacies for PMTCT. Additional strategies to reduce syphilis prevalence in the general population (such as promoting partner syphilis testing and treatment), and to reduce HIV MTCT risks (such as supporting ARV adherence in ANC), are necessary to completely meet elimination targets.

No conflict of interest
Introduction: As HIV programs are scaled-up and new activities are implemented, there is a greater need for quality assurance. Monitoring and evaluation (M&E) tools can be used to summarize programmatic data to improve delivery of patient services and guide implementation efforts. We sought to develop affordable, user-friendly, patient-level M&E tools for routine evaluation of care provided at two HIV care and treatment sites in Kinshasa, DRC, and to describe results post-initiation.

Materials and Methods: We defined indicators of key program outputs categorized into measures of productivity (N=4), data quality (N=21), and service delivery (N=25). Epi Info software was used to calculate indicators from routinely collected clinical data, and to produce lists of patients who did not receive essential services. In September 2011, Kinshasa-based staff began running the programs and disseminating quality reports and patient action lists every two weeks. We summarized program trends for the first five months post-initiation.

Results: Approximately 3,000 patients received care during the evaluation period, with an average of 35 patients enrolled and 783 clinical visits per week. Data quality improved regarding calendar date accuracy (decrease from 248 to 51 errors), mother-infant linkages (decrease from 133 to 35 missing linkages), DNA PCR result documentation (decrease from 114 to 45 tests without a documented result within two months), and breastfeeding status (decrease from 505 to 347 infants without a documented breastfeeding status at enrollment). Service delivery for HIV-exposed infants improved quickly, with increases in the proportions who received prophylactic regimens (increase from 77% to 84% receiving extended nevirapine and increase from 85% to 89% receiving cotrimoxazole by any age), as well as a DNA PCR test (increase from 75% to 86% tested by any age). Services initially delivered effectively, including ART for eligible patients and tuberculosis screening, continued to improve to over 90%. Although still infrequent, delivery of family planning services became more common (the proportion of women accessing services increased from 36% to 44%). Service delivery for exposed infants before six weeks of age remained at about 50%. The proportion of pregnant women who had a CD4 and hemoglobin measure and were started on AZT at enrollment fluctuated throughout the evaluation period, from as low as 74% to as high as 90%, with no sustained improvement. Tracking of lost patients also fluctuated with no overall improvement, with an average of about 45% of patients receiving tracking when required.

Conclusions: Routine M&E activities can improve service delivery and help prioritize improvement efforts. Processes can be automated, real-time, and coordinated locally. Patient-level indicators with corresponding accessible action lists can lead to immediate improvements in care, as well as measure aspects of implementation fidelity of new program activities. Documentation quality is essential for effective M&E systems. 

No conflict of interest

Abstract: P_97

Implementation research on PMTCT and pediatric treatment programs

Clinical outcome and mortality among HIV-infected children receiving care within the National Program in Karnataka, India

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Introduction: India continues to have a high burden of pediatric HIV infections. In 2006 the Indian National AIDS Control Organization scaled up pediatric antiretroviral therapy (ART) using specially formulated fixed-dose-combination drugs (FDCs) for children. This study aims to describe the clinico-epidemiological profile and outcomes of almost
6,000 HIV-infected children enrolled in the National Program in a high HIV-prevalence state in India.

Methods: Longitudinal data from children enrolled between 2004-2011 were obtained from 33 clinics in 20 districts in Karnataka, India. As per the national guidelines, multidisciplinary care with a deep emphasis on family counselling is provided within each clinic by a team including a doctor, nurse, counsellor, pharmacist and peer worker. In this study, children were followed for a mean period of 24 months. Statistical analysis was performed using t tests, chi square tests, ANOVA and logistic regression.

Results: Complete data from 6,075 children were obtained. Those deemed ineligible (>18 years, 77; duplicated forms, 13) were not analysed and the remaining 5,985 children were included in the final analysis. 55% were males and 74% resided in a rural area. Mean age at HIV diagnosis was 7.6 years (SD 4yrs). Eighty-eight per cent of children were in school, 10% were pre-schoolers, and 2% were school dropouts. A total of 377 (6%) were orphans who lived in residential facilities. ART was initiated in 47% (2781/5985) of the children. Mean age at ART initiation was 9.2 years (SD 4yrs). Majority of the children (74%) were on stavudine-containing regimens, and 16% were on zidovudine. Prevalence of anemia was 77%. Among those on zidovudine-containing ART, 10% developed new onset anemia, most likely zidovudine-induced anemia. Tuberculosis co-infection occurred in 533 children (9%), and was primarily pulmonary tuberculosis (81%). Among those on ART, a high level of adherence was recorded, with significant improvement of adherence over time. The proportion of children with optimal adherence (defined as >95% adherence) increased from 93% at baseline to 96% at 24 months (p<0.001). Over a mean period of 24 months, children on ART showed an increase in median CD4 from 14% (IQR 10, 19) to 30% (24, 37), while median CD4 of children not on ART remained steady at 26%. Significant CD4 improvement was observed among those with early initiation of ART and among those with optimal adherence (p<0.001). Mortality was 6%, and attrition (lost-to-follow-up) rate was 8%. Higher mortality was seen among children <6 years (OR 3.0, 95%CI 2.0, 4.4); school dropouts (OR 6.1, 95%CI 3.3, 11.0) and children with tuberculosis (OR 2.5, 95%CI 1.4 – 4.5). Children who were not on ART had a 2.3 times higher risk of death compared to those on ART, although clinical parameters and CD4 counts remained steady. Poor adherence to ART was an independent predictor of death (p<0.001).

Conclusions: Our experience highlights the role of early ART initiation and good adherence on reducing mortality among HIV-infected children. These results demonstrate that scale-up of pediatric ART services with ensuing good clinical outcomes comparable to those seen in developed countries is feasible within the Indian national program.

No conflict of interest

Abstract: P_98
Implementation research on PMTCT and pediatric treatment programs

Household follow-up of HIV-exposed infants (HEI) and their access to Early Infant Diagnostic (EID) testing – Botswana, 2011

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Background: Early Infant Diagnosis (EID) by DNA PCR at 6 weeks of age has been offered as standard of care in Botswana since 2006 for HIV-exposed infants (HEI). This critical test identifies HIV-infected infants, enabling linkages to life-saving treatment. Testing is free of charge to HEI presenting to clinics.

Methods: All HIV-positive women with singleton newborns on post-natal wards of three hospitals in the Northeast district were recruited from August-October 2010. Women agreed to be visited in their homes 2-3 months post-partum.
At household visits we asked questions about infant nutrition, health status, and access to EID.

Results: Of 203 eligible women approached, 183 (90.1%) agreed to participate in the study. We found 150 of these recruited women at home with their living, HEI (82%), who were a median 9 weeks old, and 10 (6.5%) were breastfeeding. At time of interview, only 86 (56%) infants had a DBS taken for PCR; and of these, 24.4% had received a test result at a median 10 weeks old. Of those who had been tested, but had not yet received a result, 43.2% of their mothers checked for results at clinic but results were not available. Of the HEI without a DBS taken for EID, 48.4% of mothers reported going to clinic for the test but being advised to come at another time, most commonly because staff were not available. Only 9 (6%) mothers had not yet brought their infants for EID testing.

Conclusions: Mothers we interviewed were aware of EID and brought their HEI to clinic for testing. Even in a country with relatively mature EID services, HEI presenting for testing or results may be turned away due to operational and human resource challenges at the clinic level, missing critical windows of opportunity for intervention. Quality improvement measures are needed to optimize existing services for HEI.

No conflict of interest

Abstract: P_99

Implementation research on PMTCT and pediatric treatment programs

Evaluation of feasibility and diagnostic performances of Biocentric® assays on Dried Blood Spot (DBS) for HIV-1 diagnosis in Abidjan, Côte d’Ivoire.

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Background: Early access to antiretroviral therapy (ART) in HIV-infected infants in Africa has been recommended since 2008, but remains conditioned by early infant diagnosis (EID) still not available to all on a routine basis. We evaluate the feasibility and diagnostic performances of DBS testing for EID in field conditions, in HIV-exposed infants in health clinics in Côte d’Ivoire.

Methods: Large scale pediatric screening was offered to children <3 years in five pediatric clinical sites in Abidjan from March to October 2008. For each HIV-infected child, two non-infected children were included in this study. Blood was sampled in an EDTA tube and a capillary DBS was performed for each child. The Generic HIV DNA Cell (Biocentric®, Bandol, France) kit was used to determine the HIV status, using blood from the EDTA tube. This was the reference technique. HIV-RNA levels in plasma and DBS were measured using the Generic HIV Charge Virale kit (Biocentric®, Bandol, France). Finally, HIV-DNA was also tested using the Amplicor HIV-1 DNA test version 1.5 kit (Roche®, Manheim, Germany). Sensitivity, specificity and likelihood ratios were assessed for each technique. HIV-RNA (VL) levels in plasma and DBS were compared by linear regression methods (R²) and a Bland-Altman plot.

Results: Overall, 138 HIV-exposed children, 46 infected, 92 non-infected were included for final analyses. Median viral load of the 46 infected children was 6.1 log_{10} [4.63 – 6.57]. The threshold for detectable VL RNA-HIV on DBS was 3.69 log_{10}. Among the children with detectable VL, measurements were generally higher when measured on DBS samples than plasma, differences ranging from 0 , plasma ; the to 2.5 log copies/mL. But, plasma VL was correlated with DBS viral load (R²=0.97) and average bias was -0.2 (figure). All the 4 tests were 100% sensitive and 100% specific including 100% concordance of the results obtained with the two HIV-DNA assays.
**Conclusion:** Diagnostic performances of the Biocentric® kits are completely satisfactory on DBS, and easily usable for routine EID. Although there are differences between VL measured by Biocentric® on DBS and plasma, DBS represent an interesting option to provide access to EID which is crucial to start early HIV treatment in infected babies.

*No conflict of interest*

**Abstract: P_100**

*Implementation research on PMTCT and pediatric treatment programs*

**PMTCT Performance among HIV-Exposed Infants in Tanzania**

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**Introduction:** In Tanzania, 70% of an estimated 88,000 HIV-infected pregnant women annually receive some intervention to prevent mother to child transmission (PMTCT) of HIV. Few data exist concerning the effectiveness of various treatment approaches in a field setting across a large geographic area. Dried blood spot (DBS) HIV DNA PCR testing of HIV-exposed infants was first rolled out in Tanzania in 2008. Using data gathered for DBS testing, we evaluated the prevalence of perinatal HIV transmission based on PMTCT regimen across three regions of Tanzania.

**Material & Methods:** This was a retrospective review of all mother/infant pairs enrolled in the National PMTCT program in the Arusha, Kilimanjaro, and Tanga Regions of Tanzania from January 1, 2008 to September 30, 2010. Enrollment registries at health facilities that submit DBS PCR were reviewed to document infant age, weight, feeding practice, maternal and infant PMTCT regimen, and date/result of first DBS PCR. The present analysis included mother/infant pairs for whom DBS PCR was performed at infant age ≤ 75 days. Maternal ARV regimens included: 1) none; 2) single-dose nevirapine (sdNVP); 3) sdNVP + zidovudine (combination prophylaxis); or 4) highly active antiretroviral therapy (HAART).

**Results:** Of 4,701 mother/infant pairs registered, 2,191 had a documented infant DNA PCR result ≤ 75 days of life. The overall transmission rate of HIV was 6.4%. Among HIV-infected mothers who received no therapy, transmission was 15.3%. Among mothers who received sdNVP only, transmission was 8.9%, and for those who received combination prophylaxis, transmission was 3.9%. Mothers on HAART had the lowest MTCT rate, at 2.1%. Transmission decreased significantly with sdNVP, combination prophylaxis, or HAART, compared to no treatment. The prophylaxis regimen and HAART were both significantly better than sdNVP (p<0.0001 and p=0.0002, respectively).

**Conclusions:** PMTCT regimens in resource-limited settings are effective and transmission rates are comparable to those demonstrated by clinical trials data. Use of DBS for diagnosis of HIV provides an opportunity to evaluate use and effectiveness of PMTCT regimens.

*No conflict of interest*

**Abstract: P_101**

*Co-infections in HIV-infected children*

**Impact of recent ART guidelines on incidence of tuberculosis in children with HIV in Kenya: re-evaluating the need for pre-exposure preventive therapy**

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Background: In 2008, Kenya adopted aggressive ART initiation guidelines for children similar to WHO 2010 guidelines. ART is known to reduce the incidence of TB in both adults and children with HIV. The effect of current guidelines and the impact on need for pre-exposure isoniazid preventive therapy (IPT) was evaluated.

Methods: A prospective cohort study was carried out between March 2009 and December 2010 at 3 sites with high burden of TB in Kenya: Family AIDS Care and Education (FACES)-supported clinics in Nairobi and Kisumu and New Nyanza Provincial General Hospital. Participants included HIV-infected children 6 weeks to 14 years of age without current active TB disease. Active case finding per Kenya National Guidelines occurred at study enrollment including TB score chart, chest x-ray and tuberculin skin testing. Study participants were then followed monthly to detect incident TB. Bivariate survival analysis was used to determine association between factors and time to diagnosis.

Results: After excluding 49 children (7%) with active TB at enrollment, 641 HIV-infected children were eligible for inclusion; mean age was 6.8 years (SD3.4), and 490 (76.4%) were receiving ART. Only 16 cases of incident TB were diagnosed in 722.1 years of observation (incidence rate of 2.2 per 100 child-years). In children receiving ART, those with less than 6 months of ART had a significantly increased risk of incident TB (HR 28.3; p < 0.001) compared to those with greater than 12 months of HAART. Risk of TB did not differ significantly between those with 6 - 12 months on ART and over 12 months.

Conclusions: The relatively low incidence of TB in this cohort of HIV-infected children demonstrates the protective effect of HAART to prevent TB. In similar setting with high levels of HAART use, the use of pre-exposure preventive therapy may not provide significant additional benefit.

No conflict of interest
fewer males in the HEI cohort (43% vs 51%). At entry, 125 (9%) caregivers reported having a smoking history, 62 (5%) reported current smoking, while 626 (46%) households had at least 1 current smoker. For the HEU cohort, at least marginally significant predictors of TB disease or death (unadjusted) were: baseline number of household smokers (p=0.06) and ≥5 people living in a household (HR=1.71, p=0.04); none significant after adjustment. For the HEI cohort, no smoking exposure measure was significant. Adjusting for covariates, significant predictors were: WAP z-score (adjusted HR [AHR]=0.76, p=0.002), CD4% (AHR=0.88, p=0.002), log_{10} (RNA/VL) (AHR=1.50, p=0.009), time-dependent HAART , (AHR=0.50, p=0.006) and ART-initiation at/before study entry (AHR=1.78, p=0.07).

Conclusion: Host-specific measures (CD4%,VL), ART and WAP z-score were strong predictors in the HEI cohort. WAP z-score was an important predictor of TB/death, relevant for TB screening and prevention.

A small percentage of smokers among caregivers, and no smoking intensity information on other household members, limited the exploration of smoking exposure.

No conflict of interest

Abstract: P_103

Co-infections in HIV-infected children

Selection of a 3TC-sparing ART regimen for HBV/HIV co-infected Namibian Children with normal ALT as an indicator of immune-tolerant HBV disease

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Background: It is recommended that HAART regimens for HBV/HIV co-infected patients include 2 NRTIs such as tenofovir and lamivudine which are effective in treating HBV as well as HIV in order to avoid selection of HBV resistance. However, tenofovir is contraindicated for use in pre-pubertal children. In addition, most HIV/HBV co-infected children are expected to be in the immune-tolerant phase of HBV infection, whereby despite high HBV DNA levels and presence of HBeAg, they do not need HBV treatment since the risk of liver inflammation or fibrosis is negligible. If such children require HAART, giving lamivudine as part of the NRTI backbone without tenofovir exposes them to a ~20% lamivudine HBV resistance risk per year, thus limiting future HBV treatment options. Some guidelines recommend avoiding lamivudine in such children.

Prior to initiation of HAART in Namibia, patients are tested for HBsAg, and level of alanine aminotransferase (ALT) is also determined. This study sought to establish the prevalence of HBV/HIV co-infection in children in Northern Namibia and to examine baseline ALT levels as indicators of immune tolerant vs. active phases of HBV infection.

Methods: Data were extracted from the Electronic Patient Monitoring System in five health facilities in Northern Namibia for children <18 years who initiated HAART from 2004 to February 2011. Age at initiation of HAART, gender, HBsAg result, and baseline ALT were filtered. Data was cleaned and then analyzed using EPI Info windows version.

Results: Records of 1057 patients were reviewed. 50.2% were females, and mean age was 6.4±4.7 years. Prevalence of HBV/HIV co-infection was 8.7%. Median age of the co-infected children was 12 years and 96.7% of them had baseline ALT < 2xULN, no difference from HBV-uninfected children.

Conclusion: HBV/HIV prevalence is high in our study population. Results suggest that 96.7% of HBV/HIV co-infected children do not have chronic active hepatitis. These children probably do not need HBV treatment and would likely benefit long-term from initiation of HAART with a lamivudine-sparing NRTI backbone, e.g., abacavir/zidovudine, until they reach a level of sexual maturity to allow use of tenofovir/lamivudine. Cost of abacavir for these children may be off-set by future cost savings in
Abstract: P_104

Co-infections in HIV-infected children

Early non-adherence to study drug associated with increased risk of tuberculosis in both isoniazid and placebo groups in P1041


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Introduction: P1041, a randomized clinical trial designed to evaluate efficacy of primary isoniazid (INH) prophylaxis in HIV-exposed, southern African, BCG-vaccinated infants, enrolled children 3-4 months of age with no known tuberculosis (TB) exposure. Based on data until 96 weeks, the incidence of TB was not different for those randomized to INH prophylaxis versus placebo. The purpose of this secondary analysis was to evaluate the impact of non-adherence on the results of P1041 as assessed by a detailed measurement of adherence.

Materials & Methods: Adherence to blinded study drug was first assessed at week 12 and every 12 weeks thereafter until week 96 while on study drug. Adherence was assessed by the number of doses missed in the past 3 days and whether or not a dose was missed since the last visit. Measures of adherence used for this analysis were adherence by week 12, which included any assessment recorded up to and including week 12, and adherence by week 96, which utilized all adherence assessments recorded throughout P1041. Each measure was categorized into 100% and <100% reported adherence. All TB disease outcomes through 192 weeks were considered. Hazard ratios [HR] for development of TB disease were obtained using time-to-event Cox proportional hazard modeling. These models excluded subjects with no response to an adherence questionnaire. Sensitivity analyses were conducted where non-responders to the adherence questionnaire were considered to have <100% adherence during that period, if they were still on study drug.

Results: Of the 1348 (676 in the INH group) infants with follow-up data, 1237 (92%) had a caregiver report of adherence by week 12. A total of 378 (31%) of these infants had caregivers reporting <100% adherence by week 12. Among those completing a week 12 questionnaire, the proportion of caregivers reporting non-adherence in the INH group (32%) did not differ significantly from that in the placebo group (29%) (p=0.15). Non-adherence by week 12 in the INH group was significantly associated with developing TB (HR=1.77, 95% confidence interval [CI]=1.06-2.92). The estimated HR for non-adherence was similar in the placebo group (HR=1.50, 95% CI=0.94-2.35), though the latter was not statistically significant. We found no evidence for differences in the adherence HRs between the INH and placebo groups (interaction p=0.64).

Through 96 weeks of the study, 1260 (94%) had at least one caregiver report of adherence with 69% reporting <100% adherence (68% for placebo vs. 69% for INH, p=0.65). Using this measure, non-adherence was not significantly associated with TB incidence in the INH group (HR=0.80, 95% CI=0.48-1.39).

Conclusions: Non-adherence within the first 12 weeks was associated with a greater risk of TB in P1041, but this association was not seen using non-adherence by 96 weeks. The estimated HR for non-adherence by week 12, however, was similar in both the INH and placebo groups, suggesting that the increased risk of TB may not be related to poor INH adherence, but rather the behavioral factors or exposures associated with non-adherence that may be risk factors for the poorer outcomes.

No conflict of interest
Abstract: P_105

Co-infections in HIV-infected children

Seroprevalence of HBV and HCV among Children in the Kilimanjaro Region of Tanzania

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Introduction: Data on HIV and hepatitis B virus (HBV) and hepatitis C virus (HCV) co-infection among children in Africa are scarce. We evaluated the seroprevalence of HBV and HCV among healthy HIV-uninfected children and HIV-infected children in the Kilimanjaro Region of northern Tanzania.

Material & Methods: HBV and HCV markers were assessed on banked serum and plasma samples from HIV-negative children ages 1 month to 18 years and HIV-infected children on highly active antiretroviral therapy (HAART) a minimum of six months from 1 to 16 years of age. HBV markers included hepatitis B surface antigen (HBsAg), hepatitis B surface antibody, and hepatitis B core antibody (HBcAb). Infection was defined as a single positive HBsAg or HBcAb result. HCV infection was assessed by anti-HCV ELISA. Validation studies were performed on all assays prior to use and all were FDA-approved.

Results: Samples from 560 children were available for testing. Of 394 HIV-negative children, 36 (9.1%) were HBV-infected, and of 161 HIV-infected children, 33 (20.5%) were HBV-infected. Children with HIV were 2.6 times more likely to be HBV positive (95% CI 1.53, 4.29) than children without HIV (p=0.0002). None of the 560 samples was positive for anti-HCV antibody.

Conclusions: HBV seroprevalence is high among children in the Kilimanjaro Region, with a significantly higher prevalence among HIV-infected children. Routine screening for HBV should be performed among HIV-infected children. Patients with co-infection require closer monitoring of liver transaminases due to hepatic toxicities associated with antiretroviral therapy, and must be provided with appropriate HAART which will target both viruses. Catch-up immunization with HBV vaccine should be considered for older HIV-infected children.

No conflict of interest

Abstract: P_106

Co-infections in HIV-infected children

Seroprevalence of Hepatitis B in a Cohort of HIV-Infected Children and Adults in Swaziland

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Introduction: Hepatitis B virus (HBV) is an important co-morbidity in the HIV epidemic. All new HIV-positive children and adults at the Baylor College of Medicine Bristol Myers Squibb Children’s Clinical Center of Excellence in Mbabane, Swaziland are screened for HBV surface antigenemia. Few data are available regarding HBV-HIV co-infection in sub-Saharan Africa, especially in children. The purpose of this study was to understand the burden of HBV co-infection in our patients.

Materials & Methods: A retrospective chart review of patients enrolled from 1/1/2009–5/31/2011 was conducted. HIV-positive, ART-naïve patients were included. Demographic and lab data from time of enrollment were recorded. The seroprevalence of HBsAg in children and adults was calculated and the data were analyzed using the Mann-Whitney U test for continuous variables or Fisher’s exact test for dichotomous variables, to evaluate for
differences in ALT levels and immunosuppression between the HBsAg-positive and negative individuals.

**Results:** 1282 patients had HBsAg results documented and were included in analysis. 500 were children <15 years. 7 (1.4%) of the children and 40 (5.1%) of the adults were HBsAg-positive. Prevalence in under-5s was low (0.4%). Among adult females, prevalence was 4.2% and among adult males it was 9.8% (p=0.022). The median ALT level was 19 U/L in the HBsAg-negative adults and 25 U/L in the HBsAg-positive adults (p=0.005). 138 pregnant women were included, and 5 (3.6%) were HBsAg-positive.

**Conclusions:** The seroprevalence of HBsAg in this cohort of HIV-infected children and adults in Swaziland was found to be 3.7%. Few children were found to be HBsAg-positive, which is encouraging as Swaziland has surpassed 80% HBV vaccine coverage for the past 15 years. Given the number of patients found to be HBsAg-positive, especially among adults, it is important for ART programs to strategically utilize appropriate medications that have been found effective in treating patients with HBV-HIV co-infection.

*No conflict of interest*

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**Abstract: P_107**

**Co-infections in HIV-infected children**

**Prevalence of HIV-related Dental Disease in Children at the Botswana-Baylor Children´s Clinical Centre of Excellence (COE) in Gaborone, Botswana**

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**Background:** While HIV-associated dental disease and oral lesions are responsible for considerable morbidity amongst HIV-infected children, improved oral health is associated with improved mental and physical health, making an understanding of the relative prevalence of these conditions important in targeting interventions. There is paucity of such data in Botswana. This study assesses the prevalence of HIV-associated dental disease and oral lesions diagnoses in HIV-infected children attending the COE, a large government-affiliated paediatric HIV treatment centre.

**Methods:** A retrospective chart review of children ages 0-19 years attending the COE between January 2008-December 2011 for dental disease and oral lesions as defined by presumptive criteria of EEC Clearinghouse,1993.

**Results:** Of the 1832 active patients at the COE, only 84 patients were identified as having paediatric dental issues, giving a prevalence rate of 4.6%. 31 were female(37%) with an average age of 11 years(3 months-19yrs). Dental Caries (n=69, 82%) was the most common lesion followed by oral sores(including herpes labialis, aphthous ulcers)(n=10; 11.9%) and oral candidiasis (n=5; 6%). Only 54 (61%) in the group had recent lab results, with an average CD4 of 987(237-2112)/ 34%(11%-49%). All patients were virologically suppressed.

**Conclusions:** Even with the virologic suppression imparted by effective antiretroviral treatment, amongst children with oral manifestations dental caries were common. The lack of dental caries-CD4 association is consistent with paediatric and adult data from other settings, and reinforces the suggestion that ART alone has limited impact in addressing dental disease in HIV-infected children. Fluoridation of drinking water in Botswana may reduce the prevalence of paediatric dental caries, as would promoting improved oral hygiene and reduced consumption of sugary snacks and drinks. This problem needs to be characterized further in larger, prospective studies.

*No conflict of interest*
Abstract: LB_02

Intimate relationships in young people with perinatally-infected HIV: An Interpretative Phenomenological Analysis

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Background: The availability of HIV testing and anti-retroviral medication for pregnant women has led to a marked reduction in perinatal transmission of HIV in recent years, in the developed world. Indeed, the incidence of children aged 13 and under being diagnosed with HIV decreased by over 90% between 1992-2003 in the US (Centers for Disease Control and Prevention, 2005). Due to such developments in diagnosis and medication, young people with perinatally-infected HIV in developed countries have been surviving in greater numbers into late adolescence and young adulthood. In the UK, therefore, individuals with perinatally-infected HIV are now mostly adolescents and young adults who were infected a number of years ago. This cohort are facing normative challenges in terms of their intimate relationships and procreational intentions, in addition to the numerous difficulties related to living with, and growing up with, HIV. The majority of previous studies into this population have investigated rates of sexual behaviour, with a smaller number having examined the subjective experience of relationships. These latter studies have also been limited in including particularly young samples and focusing on facets of relationships in isolation. The present study examined, in depth, the experiences of intimate relationships in perinatally-infected young adults and how participants regarded aspects of having grown up with HIV, specifically, to have impacted on their experiences regarding relationships.

Materials and Methods: Participants were recruited from an NHS clinic in London where patients aged 16-25 years old are seen for the monitoring and management of their HIV by a multi-disciplinary team. Seven participants aged 18-23 years old were interviewed in depth about their experiences of growing up with HIV and intimate relationships. The transcript data was analysed according to the principles of Interpretative Phenomenological Analysis (IPA; Smith, Flowers, & Larkin, 2009). For each transcript in turn, a basic initial coding was undertaken, followed by descriptive/phenomenological and interpretative analysis. In addition to this idiographic focus, the individual themes were examined together to establish conceptual links and develop a set of master/subordinate themes. Participants also completed the Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983) and the Rosenberg Self-Esteem Scale (RSES; Rosenberg, 1965).

Results: Six master themes emerged: (1) HIV as a secret within relationships (2) Strategies within relationships (3) Partner attitude to HIV and disclosure (4) Characteristics of partners (5) Positive responses to disclosure (6) Having children of one's own. Strong links were apparent between participants’ own experiences of growing up with HIV, for example having been disclosed to themselves and HIV-related stigma, and their approach to intimate relationships.

Conclusions: The results have strong clinical implications for services providing support to this population in terms of specific aspects of intimate relationship experience to be discussed with patients. It appears particularly important that a proactive approach is adopted with those young people who may otherwise be more socially-isolated. Suggestions for future research, based on the present thematic findings, include dyad studies of HIV-positive young people and their partners to elucidate the experience of being in an HIV-affected relationship.
Abstract: LB_03

Prevention of Mother to child HIV – transmission in Saudia Arabia’s Western Province: An 8 – years review

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Background: While the prevalence of human immunodeficiency virus (HIV) infection in Saudi Arabia is low, identification of HIV infected pregnant women and implementation of prevention of mother – to – child transmission (PMTCT) programs remain a challenge. The purpose of this review was to assess PMTCT in the western province of Saudi Arabia.

Method: A retrospective review of medical records from the last 8 years (2004 to 2011) was conducted of all HIV positive pregnant women at King Saud Hospital. All 100 babies born to 74 HIV infected women, who were managed according to the three-step PACTG-076 approach, were tested for HIV using ELISA and RNA-PCR.

Result: All 100 infants remain HIV negative. A total of 53 women (72%) had one infant and one set of twins were identified; the other 21 women (28%) had either 2 or 3 babies after they had acquired HIV infection. Of the 100 babies, 88 were delivered vaginally and 12 by Caesarian Section for obstetric reasons. Five of the babies were preterm (33-35 gestational weeks) while the remainder were full term. Ninety three babies had exclusive bottle feeding; the remaining 7 babies were breast fed for a periods ranging from 2 to 9 months. Twenty of the children, who have reached school-going age, have entered school and are performing well.

Conclusion: The PMTCT program at King Saud Hospital in Saudi Arabia has successfully eliminated HIV transmission to babies since 2004.

Abstract: LB_04

Reviewing progress: Trends in characteristics of pediatric patients attending HIV care and treatment clinics in Tanzania and Zanzibar over 7 years.

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Background: Pediatric HIV care and treatment programs have scaled-up in recent years, particularly in Africa. Initiation of antiretroviral therapy (ART) during infancy and early childhood and with less advanced HIV disease leads to better long-term outcomes, and WHO recommends ART initiation upon HIV diagnosis in children <2 years. As HIV service programs mature, and considering the challenges of pediatric HIV diagnosis and enrolment, it is important to assess whether there are improvements in enrolling HIV-infected children into care and starting ART earlier.

Methods: The Optimal Models study is a prospective open cohort study of patients attending ICAP-supported HIV clinics and utilizes secondary analyses of routinely collected patient and site level data. This analysis explored trends in pediatric (<15 years) patient characteristics of children enrolled from January 2005 to December 2011 at 44 clinics in 3 regions of mainland Tanzania (Kagera, Kigoma, Pwani) and Zanzibar. Descriptive comparative statistics were computed for differences in characteristics of patients enrolled in 2005-2007, 2008-2009 and 2010-2011.

Results: A total of 4,699 children were enrolled: 1,229(26%) in 2005-2007, 1,877(40%) in 2008-2009 and 1,593(34%) in 2010-2011. A total of 2,479(53%) children were female, 4,552(97%), were from mainland Tanzania and 147(3%) from
Zanzibar. Median age (years) at enrolment decreased from 6.1 (IQR:2.7-10.0) in 2005-2007 to 4.8 (IQR:1.9-8.6) in 2008-2009, and 4.1 (IQR:1.5-8.1) in 2010-2011 (p<0.0001), and children <24 months at enrolment increased from 227(18%) to 491(26%) and 501(31%) (p<0.0001). Prevention of mother to child HIV transmission (PMTCT) programs contributed 75(6%) children in 2005-2007, 188(10%) in 2008-2009, and 220(14%) in 2010-2011 (p<0.0001). In 2005-2007, 513(63%) of the children were WHO stage III and IV at enrolment compared with 867(51%) in 2008-2009 and 614(41%) in 2010-2011 (p<0.0001). Among the 2,318 children >5years, 282(39%) enrolled in 2005-2007, 364(40%) enrolled in 2008-2009 and 295(43%) enrolled in 2010-2011 had a CD4 count at enrolment, and 219(30%), 276(30%) and 165(24%) respectively had a CD4 count at ART initiation. Median CD4 count at enrolment increased from 378/ul (IQR:123-697) in 2005-2007 to 401/ul (IQR:172-718) in 2008-2009 and 451/ul (IQR:198-744) in 2010-2011 (p=0.04), and median CD4 count at ART initiation was 208/ul (IQR:107-402) and 223/ul (IQR:60-396) in the respective time periods (p=0.36). Of all the children enrolled in 2005-2007, 2008-2009 and 2010-2011, 742(60%), 1,045(56%) and 812(51%) started ART (p<0.0001); 295(40%), 413(39%) and 212(26%) initiated d4T-containing regimens and 440(59%), 632(60%) and 573(71%) initiated AZT-containing regimens respectively (p<0.0001).

Conclusions: Over time, HIV clinics in Tanzania and Zanzibar enrolled younger children, and children with less advanced HIV disease. More children are being identified through PMTCT programs. However, many children were missing documentation of CD4 counts at enrollment and ART initiation, with no increase in median CD4 count at ART initiation over time- areas that deserve further focus in program enhancements. The decline in d4T use could be reflective of recent recommendations to limit use of this drug, but a substantial proportion of children continue to initiate d4T-containing regimens.

Abstract: LB_05
Implementation of Comprehensive Pediatric HIV Services in a Resource-Limited Setting in Nigeria: FCTA/MDH experience

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Background: Pediatric HIV is a problem of developing countries with about 90% of cases acquired through MTCT (mother to child transmission). It is associated with high morbidity and mortality, interventions have been shown to reduce transmission, mortality and also improve survival.

In 2004, Maitama District hospital (a Federal government owned health facility) began PMTCT services which were initially funded by an indigenous organization (Gede foundation). However, by May 2005, Family Health International/Global HIV/AIDS Initiative Nigeria (now Strengthening Integrated Delivery of HIV/AIDS Services-SIDHAS) a USAID PEPFAR funding IP, took over the PMTCT services support. By January 18th 2007 Comprehensive HIV services was implemented in the hospital. Challenges to initiation and implementation of comprehensive pediatric HIV services include: High rate of home delivery, Limited access to HIV testing and care, Shortage of personnel and exclusion of nursing staff from point of service testing, Limited laboratory capacity at the hospital level, under developed medical record system, Weak inter and intra-facility referral systems and Limited linkages to community based resources and HIV related stigma and discrimination

Objectives: General Objective: To provide comprehensive pediatric HIV services to survival and quality of life among infected children through a number of interventions.
Specific Objectives:
• Implement PICT 'opt out' strategy
• Improving uptake of Pediatric services
• Provide ARV prophylaxis and ART to exposed and infected children
• Develop functional systems to ensure quality clinical management of HIV infected children

Methods / Interventions: In collaboration with FHI/GHAIN, the following interventions were implemented:
1. Provided hands-on facility-based PMTCT and rapid HIV testing training for antenatal and maternity staff
2. Established Provider-initiated HIV testing and Counseling (PITC) ‘opt out’ approach
3. Carried out capacity building of staff in all areas of PMTCT and pediatric HIV
4. Improved service delivery
5. Strengthened intra- and inter- facility linkages, and community-facility linkages

Results: From April 2007 – Dec 31st 2011 total hospital deliveries were 10,376 of which 1146 (11.04%) were positive deliveries. However only 687 HIV exposed infants (HEIs) had DBS done out of which 58 (8.4%) were DBS positive. Total number of children with HIV enrolled within the same period was 258 of which 106 were on HAART and 126 were on care as they were not eligible for ART. There are 7 children with HIV and TB co infection. Majority of the children are on 1nt line ARVs. The outcome by the end of Dec 2011 showed that 27 have defaulted, 15 were LTFU, 1 had ART stopped and 3 were transfer out.

Conclusion: Although pediatric ART has commenced in Nigeria, far too few children currently have access to care. The programme requires the participation of all stakeholders in the public and private sectors as well as the civil society organizations.

Abstract: LB_06

Reducing Maternal and Neonatal Mortality in Zambia – A Rapid Implementation of the Campaign on Accelerated Reduction in Maternal Mortality in Africa

(CARMMA) Leveraging Experience from PMTCT.

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Background: Globally over 500,000 women die in childbirth or from complications during pregnancy each year, the majority of them in Africa. Infant mortality remains unacceptably high in Africa as well. Zambia adopted the Campaign on Accelerated Reduction in Maternal Mortality in Africa (CARMMA) as national policy in 2010. In 2007, the maternal mortality ratio in Zambia was 591 maternal deaths per 100,000 live births, one of the highest in the world. Limited progress to reduce maternal and neonatal mortality has been made in Zambia since the adoption of CARMMA. There are few data on the impact on neonatal mortality from programs specifically targeting maternal mortality reduction. Recent data from Africa suggest that effective prevention of maternal to child transmission (PMTCT) programs may have a positive impact overall maternal health indicators, even in non-HIV infected women.

Methods: Maternal Mortality reduction within the Global Health Initiative (GHI) is a new United States Government (USG) initiative launched in October 2011 with an aim to reduce by 50% maternal mortality in four demonstration districts (population 887,711, estimated pregnancies 47,933) in Zambia in 15 months by focusing on the critical 24 hour period surrounding delivery. A secondary target is reduction in neonatal mortality. The program is integrated into the USG’s GHI for Zambia and coordinates the work of the Zambian Ministry of Health and the USG global health platforms: PEPFAR’s HIV programs; USAID’s Maternal and Child Health Programs; US Peace Corps Volunteers; and US Department of Defense HIV programs. Evaluation will include community and facility maternal mortality determination and signal function indicators.
Abstracts

Results: In the first 4 months of the program, detailed surveys of all 96 health facilities have been completed; identifying strengths and gaps with regard to equipment personnel and training, medical supplies, transportation, and communication. A full enumeration of all households with identification of maternal deaths in the past 12 months utilizing verbal autopsy is just completed and shows substantial variation by region and poor correlation with official estimates. Resources from 18 implementing and cooperating partners have been identified, coordinated, and mobilized.

Conclusions: Reduction in maternal and neonatal mortality in Africa has been disappointingly slow. Through an intensive and rapid effort coordinating available resources and using lessons learned from PMTCT, the initiative aims to make a swift, significant and sustainable reduction in maternal and neonatal mortality.

Abstract: LB_09

Efavirenz Sprinkled and Liquid Formulations with Didanosine and Emtricitabine in HIV-1-infected Infants and Children 3 months to 6 years of Age

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Background: The ongoing AI266922 study is an open-label, single-arm, dose-ranging phase 2 study assessing the pharmacokinetics (PK), safety and efficacy of efavirenz (EFV) capsule and oral solution formulations in combination with emtricitabine (FTC) and didanosine (ddI) in infants and children aged 3 months to 6 years.

Methods: Antiretroviral-naïve and experienced HIV-1-infected pediatric individuals with HIV RNA ≥1,000c/mL received sprinkled capsules (mixed with a small amount of food vehicle) or liquid EFV (using dosing algorithm) given once daily plus FTC(6mg/kg)+ddI(240mg/m²). The need for EFV dose change/switch to EFV sprinkle was determined by PK analyses at weeks 2, 10, and 18. Safety and efficacy outcomes at 48-weeks are reported.

Results: A total of 37 subjects (median age 0.7 years, 65% male, 65% Caucasian) were treated with EFV. At baseline, median plasma HIV-1 RNA was 5.88 log₁₀ copies/mL, median CD4+ cell count was 1144 cells/mm³ and median CD4+ percentage was 25%. Median time on study therapy was 60 weeks. At Week 2, 14/33 subjects with evaluable PK exhibited values below projected concentrations and required higher EFV dose, while 6/33 subjects required a decrease in EFV dose due to higher than projected levels. Ten of 37 subjects (27%) discontinued before Week 48. By Week 48, the proportion of subjects who achieved HIV RNA <400 c/mL and <50 c/mL, using the virologic response-observed cases analysis, was 77.8% and 63%, respectively. Using the confirmed virologic response analysis, the proportion of subjects who achieved HIV RNA <400 c/mL and <50 c/mL was 56.8% and 48.6%, respectively. Subjects in all age groups achieved median reductions in log₁₀ HIV RNA from baseline that ranged from -2.92 c/mL to -3.27 c/mL, with a median of -3.18 c/mL by Week 48. The median increase from baseline in CD4+ count was 196 cells/mm³ and median increase in CD4+ percentage was 6%. There were no new or unexpected safety events. Two deaths were reported after treatment, neither was considered treatment-related. Two (5.4%) patients discontinued due to AEs. Serious adverse events were reported in 20 of 37 treated subjects (54.1%). The most common AEs were diarrhea (49%), nasopharyngitis (35%), pneumonia (30%), and pharyngitis (27%). The incidence of neurologic events and rash were 10.8% and 21.6%. The majority of hematologic and liver function abnormalities were Grade 1 to Grade 2.

Conclusion: EFV given once daily was efficacious in this pediatric population aged ≥3 months to <6 years with no new safety findings.
reported compared to the known safety profile of EFV.

Abstract: LB_10

Risk and Resilience in Perinatally HIV-infected and Perinatally HIV-exposed, uninfected adolescents

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Background: Research with perinatally HIV-infected (PHIV+) youth has prioritized identifying poor health and behavioral outcomes. However, as PHIV+ children increasingly survive into adolescence and young adulthood, understanding positive development may be equally important in informing preventive interventions. This study examines critical domains of positive development in addition to risk behaviors in PHIV+ youth compared to perinatally HIV-exposed, uninfected (PHIV-) adolescents.

Methods and Materials: Data come from the third wave of a U.S longitudinal study of behavioral health in perinatally HIV-exposed youth, ages 9-16 years at baseline and 13-22 years at third wave interview (n=218; 61% PHIV+; 51% female; 49% African-American; 35% Latino; 43% living with HIV+ caregivers). Demographic characteristics included youth age, gender, race/ethnicity, youth’s relationship to caregiver (biological vs. adoptive), HIV status, and household composition and income. Items from the National Educational Longitudinal Survey (NELS) were used to obtain education and employment information. Youth psychiatric and substance use disorders were assessed using the Diagnostic Interview Schedule for Children (DISC-IV) which generates DSM diagnoses and can be administered by lay interviewers. The Adolescent Sexual Behavior Assessment was administered via ACASI to assess sexual initiation, risk, and pregnancy. Chi-square test was used to compare the HIV+ youth with the HIV- youth on their demographics, risk behaviors, and resilience outcomes.

Results: Both PHIV+ and PHIV- youth were from high-risk backgrounds, primarily inner city impoverished communities, with 42% living with a single parent and approximately a third reporting problems with basic living needs. High rates of psychiatric disorder (44%) and experience of some remedial education (46%) were found with no HIV-status group differences. However, PHIV+ youth were more likely to have a substance use disorder (18% vs. 5%, p=.029). In spite of vulnerabilities in both groups, rates of sexual initiation (52%), unprotected sex (27%) and pregnancy (17%) were the same or below same-age US peers (e.g., Youth Risk Behavior Surveillance System). Moreover, across both groups, 39% reported no risk outcomes (psychiatric disorders, unsafe sex, substance use disorder) and 61% were at age-appropriate grade level, with no HIV-status differences. Among youth > 18 years of age (n=85), a majority graduated high-school (62%); half worked in the past year (51%); and 22% lived independently (no HIV-status differences). Age was a consistent predictor of risk behavior. Gender differences were found only in rates of sexual initiation (59% boys vs. 44% girls; p=.041) and STDs (3% boys vs.14% girls; p=.011), with no race/ethnicity differences.

Conclusions: Data suggest resilience in spite of engagement in some high risk behaviors in both PHIV+ and PHIV- youth who are primarily from high-risk backgrounds. Resilience frameworks that examine family and psychosocial predictors of positive development may be important to developing much needed evidence-based interventions for both PHIV+ and PHIV- youth.
Abstract: LB_11

Barriers to Delivery of EID Results to Caregivers in MNCH settings in Swaziland

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Background: Despite strengthened testing of HIV-exposed infants in Swaziland, challenges remain in delivering early infant diagnosis (EID) results to caregivers in maternal, neonatal, and child health (MNCH) clinics. In Swaziland, HIV prevalence among pregnant women is 41.1%, testing of HIV-exposed infants by 8 weeks is 55%, but only 28% of tested infants receive their EID results within 8 weeks of testing. In 2011, the Elizabeth Glaser Pediatric AIDS Foundation conducted a rapid assessment at four antiretroviral therapy (ART)-MNCH clinics to understand barriers to delivery of EID results to caregivers.

Materials & Methods: The assessment was conducted using a cross-sectional, descriptive design using May-August 2011 data from caregivers of HIV-exposed infants attending their second immunization visits at child welfare clinics (CWC). Health care workers were trained on administering the semi-structured questionnaire to caregivers. After explaining the assessment, caregivers who consented were interviewed by MNCH nurses.

Results: A total of 105 caregivers participated in the assessment, ranging in age from 18 to 44 years, (mean age of 27.97) and 92.4% were aware that their infants were HIV-exposed. Of them, 94 (97.1%) had been informed about EID and 86 infants (91.4%) had undergone dried blood spot (DBS) DNA PCR analysis at the first immunization visit at 6 weeks while 19 infants (18%) had not been tested. Of the 86 caregivers of DBS-tested infants, 22 (25.5%) did not receive their results at the time of assessment. These 22 caregivers responded to the questionnaire with the following reasons why the results were not received:

- The result was not ready when the caretaker returned to the clinic (48%);
- Fear of not knowing if the child’s status will be negative (26%);
- Fear the child will not live after testing positive (13%); and
- Fear the child’s father would not approve of the child taking ARVs since he does not allow the mother to take ARVs herself (9%).

All 105 caregivers were asked how the clinic could better promote DBS testing and encourage caregivers to collect their results; 120 responses were collected; the most frequent included:

- Give continuous health education during antenatal care and at CWC (33%);
- Provide same-day DBS results (27%);
- Call when results are back (15%)
- Explain the benefit of EID (11%);
- Give appointment dates to collect results (8%);
- Nurses should speak politely (3%); and
- Remind caregivers of DBS at first CWC visit (2%).

Conclusions: In order to increase uptake of EID test results by caregivers and reduce the number of exposed children missed for DBS testing, our study found several potential interventions, including: strengthening the quality and frequency of EID counseling at all PMTCT points of care; involving fathers in EID; reconfirming appointments and rescheduling when results are not ready; and, actively following clients to collect EID results to reduce fear of receiving results.. These findings will be shared with regional and site counterparts to advocate for more comprehensiveness and sensitivity to caregiver concerns related to fears and convenience of receiving EID results.

Abstract: LB_12

The acceptability and use of pillboxes within a paediatric population in resource limited settings – the ARROW trial experience
Background: Challenges to adherence for children and adolescents taking antiretroviral therapy (ART) in resource-limited settings include travelling between caregivers, administration of ART at school and issues of confidentiality. Pillboxes allowing tablet regimens to be organised into daily doses may be more convenient and discreet than single/multiple bottles. However, there is limited information on their usefulness and acceptability.

Methods: ARROW (AntiRetroviral Research for Watoto) is a randomised trial of ART monitoring and treatment strategies in children and adolescents in Uganda and Zimbabwe. Those taking tablets (based on weight-band dosing) received a pillbox that detached into daily boxes, which was demonstrated by the trial nurse. Questionnaires were administered to caregivers 4, 24 and 48 weeks after pillbox receipt to assess its use and acceptability.

Results: Pillboxes were received by 962 children/adolescents, and questionnaires returned at clinic visits by 639 (66%) caregivers at week 4, 530 (55%) at week 24 and 536 (56%) at week 48. Missing caregiver questionnaires was commonly related to older children attending clinic visits without caregivers. For children/adolescents whose caregivers returned one or more questionnaires, the median (IQR) [range] age at which the pillbox was dispensed was 7.4 (4.7-10.7) [1.9–19.1] years. Over the three assessments, a mean of 67% of caregivers reported always, 19% sometimes and 14% never using the pillbox (similarly over time). The main reason for its use (60% of caregivers) was a reminder to take ART with 73% finding it made it easier to administer the correct dose. 11% and 16% of caregivers reported using the pillbox because the child or the caregiver respectively had travelled. An increasing proportion over time reported that it made it easier for the child to travel (24% at week 4 rising to 39% at week 48). Overall a mean of 55% of caregivers reported improvements in their child’s adherence following pillbox receipt. Most primary caregivers (74%) preferred the pillbox to separate tablet bottles, reporting that it was convenient (79%), discreet (72%) and easy to use (84%), and that most (66%) other caregivers also preferred it. 81% said they would recommend its use to others.

Conclusions: Pillboxes were accepted by caregivers in these resource-limited settings as a readily used vehicle for administering ART to children. Improvements in adherence, anecdotally reported here, need to be confirmed by pill count and other adherence data collected in the ARROW trial. Whether children had similar or different perceptions can be explored in parallel questionnaires administered to children > 7 years at the same time points.

Abstract: LB_13

Evaluation of a rapid point-of-care test to screen for HIV infection in infants

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Background: Infant HIV diagnosis is complicated by transfer of maternal antibodies during pregnancy and breastfeeding and inconsistent / delayed antibody production in infants. The WHO recommends using RNA- or DNA-based assays for HIV diagnosis in children <18 months of age. However, those assays have long turn-around-times and are unavailable and unaffordable in many settings. We evaluated the
INSTI HIV-1 Antibody Test (bioLytical Laboratories, Inc.) for detection of infant HIV infection. This assay uses IgG-specific protein A to detect anti-HIV antibodies, provides results in ~1 minute, and is FDA-cleared for use with whole blood, plasma, and serum.

**Materials and Methods:** Samples were obtained from infants in the Post-Exposure Prophylaxis (PEPI)-Malawi study which evaluated antiretroviral regimens to prevent post-natal HIV transmission. Infants were enrolled at birth and followed for up to 24 months. Most women (~90%) breastfed for 6 months; breastfeeding beyond 6 months was more frequent in women with HIV-infected infants. Infant HIV infection was diagnosed by DNA PCR testing through 15 months, and EIA / Western blot starting at 18 months of age. Plasma samples (n=675) from 250 infants aged 3-24 months were tested (77 HIV-uninfected and 173 HIV-infected infants [86 infants with in utero infection, 87 infants who were HIV-infected after birth by 24 months]). Technologists performing the INSTI test did not know the infants’ infection status. Sensitivity and specificity of the INSTI test were measured by proportions. PEPI HIV infection status at each visit was the gold standard. Generalized estimating equation (GEE) logistic models assessed association of PEPI HIV status, breastfeeding, and age with INSTI test results.

**Results:** At 14 weeks, most infants (13/15) had reactive INSTI test results regardless of infection status. At 6 months, the sensitivity and specificity were 94% and 79%, respectively. At 9, 12, and 15 months, sensitivity ranged from 86% to 94% and specificity was 98%. At 18 and 24 months, sensitivity was 94-95% and specificity was 100%. From 9 to 15 months, there were 3 false positive results (2 for the same infant) and 21 false negative results (4 infected infants had repeatedly negative test results, accounting for 9/21 false negative results). In a multivariate GEE model that included infant age and current breastfeeding status, positive INSTI test results were strongly associated with PEPI diagnosed HIV infection (adjusted odds ratio [aOR]: 189.0, 95% confidence interval [CI]: 89.1-401.1.) and moderately with older age (aOR: 0.91 / month, 95% CI: 0.85-0.98). INSTI test results were not independently associated with ongoing breastfeeding (aOR: 1.04, 95% CI: 0.44-2.43).

**Conclusions:** The INSTI HIV-1 Antibody Test was not suitable for use in infants 14-weeks and younger. However, the test typically had sensitivity >90% and specificity >95% in children 9-15 months old; specificity was somewhat lower in 6-month old infants. This point-of-care test provides a rapid, cost-effective method for screening infants for HIV infection, and may be useful in resource-limited settings. Further work is needed to evaluate the performance of this test for infant HIV screening in different cohorts and using whole blood samples obtained by heel stick.

**Abstract: LB_14**

**The VUKA Family Project: A Family-based Mental Health and HIV Prevention Program for Perinatally HIV-infected Youth**

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**Background:** Improved access to antiretroviral treatment (ART) in high HIV seroprevalence countries has led to a growing population of perinatally HIV-infected (PHIV+) children reaching adolescence. Although studies of this population have found poor health and behavioral outcomes, including ART adherence, there are few evidence-based interventions to support families in promoting the psychosocial well-being of PHIV+ youth and preventing secondary HIV transmission to others. We present data from a pilot randomized controlled trial of a family-based mental health and HIV prevention program in KwaZulu-Natal, South Africa (SA).
Methods and Materials: Informed by Social Action Theory and adapted from the CHAMP program, The VUKA Family Project was developed for PHIV+ youth, 10-14 year olds, and their caregivers receiving care in two SA hospitals using community-based participatory methods. A 10-session cartoon-based curriculum focused on loss and bereavement, HIV knowledge, disclosure and stigma, coping and mental health, ART adherence, family functioning and support, and risk prevention was piloted with 65 families randomized to VUKA or Standard of Care (SOC). This multiple family group intervention was led by lay counselors under the supervision of a psychologist.

Baseline and post-test assessments were conducted. Measures translated and back-translated of adherence, mental health, family functioning, stigma and support were administered to all participants. Very good-excellent reliability of most of the measures has previously been demonstrated in South African. Generalized linear model (GLM) was used to compare VUKA families to SOC families on changes in key outcomes overtime. Generalized estimating equation (GEE) was employed to account for the effect of repeated measures. We report the group difference (VUKA vs. SOC) in changes overtime on outcomes (i.e., the regression coefficient (beta) obtained from each of the GLM models) as well as its corresponding p-values.

Results: Data indicate high levels of feasibility and acceptability of VUKA with 94% attending ≥ 8 of 10 sessions. VUKA participants improved in all psychosocial domains. Findings suggested some significant group differences and trends in key areas. Compared to SOC participants, VUKA youth had significantly greater improvement on ART adherence (beta=1.53, p=0.05) and caregiver-child communication comfort (beta=0.80, p=0.002). VUKA group also demonstrated a trend of greater increase on youth HIV treatment knowledge (beta=1.00, p=0.08), caregiver-child communication frequency (beta=0.48, p=0.09), and a greater reduction on caregiver external stigma (beta=-0.48, p=0.09).

Conclusions: VUKA shows promise as a family-based mental health and prevention program for PHIV+ youth that can be delivered by lay staff in medical care settings-- a task-shifting approach, critical to low resource settings. Data suggest that a theory-driven intervention focusing on self and social regulation (primarily through the family) may improve youth health and mental health.
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ABSTRACTS

Abstract book - only
Abstract: AB_01

HIV infection and adolescents

Not Big Children, Not Little Adults: Results from a Training of Trainers on Comprehensive Adolescent-Friendly HIV Services in Rwanda

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Introduction: Young people are at the center of the HIV epidemic: 5 million youth aged 15–24 are currently living with HIV, 76% residing in Africa. Adolescents living with HIV (ALHIV) are a diverse group who face unique developmental, clinical, psychosocial, adherence, and sexual health challenges requiring innovative public health strategies.

Material & Methods: In December 2011, selected Modules of the ICAP Adolescent HIV Care and Treatment: A Training Curriculum for Health Workers, were piloted in a training of trainers (TOT) at CHUK in Rwanda. Participants included 15 multidisciplinary health workers (HWs) and 3 adolescent “co-trainers.” A number of topics were covered, such as the nature of adolescence and provision of youth-friendly services, clinical care, counseling and communication, and sexual and reproductive health services.

Results: The adaptation of innovative and ALHIV-specific training content and participatory methodologies resulted in a successful TOT and development of action plans to scale-up ALHIV services. Adolescent co-trainers provided insights on the training content and youth-friendly services, based on their own experiences – a creative application of the meaningful involvement of PLHIV principles. After the 5 day training, pre- and post-test scores showed improved knowledge of ALHIV care: Pre: 4.6/12 (38%), Post: 7.6/12 (63%).

Evaluations highlighted innovations: “this was my first time thinking about adolescent vulnerabilities and sexuality;” the benefits of adolescent participation: “I appreciate that adolescents participated so we learn what they need;” and empowerment of adolescent co-trainers: “today I learnt that before we start taking meds they [HWs] should talk to us about it.”

Conclusions: Training content and methodology allowed for insightful participation of adolescent co-trainers, contributing to HWs commitment to implement comprehensive and developmentally-appropriate services for ALHIV. The generic ICAP adolescent care and treatment training package is a unique resource that can contribute to the scale-up of comprehensive, quality services for ALHIV in Rwanda and globally.

No conflict of interest

Abstract: AB_02

HIV infection and adolescents

An innovative way to improved sexual, reproductive health and HIV care for adolescents living with HIV: role of non-caregivers

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Introduction: Successful scale up of paediatric HIV care services has resulted in a large number of children growing into adolescence and adulthood in Zambia. There is an urgent call for strengthening of care and support for those adolescents.

Methods: In order to explore people’s attitudes towards adolescent HIV care, the Ministry of
Health Zambia conducted a country wide survey targeting 35 randomly selected health facilities offering paediatric HIV services. Face-to-face interviews were conducted with clients attending ART clinics in these facilities.

Results: A total of 332 clients (254 female) were interviewed. Of those 133 (40.1%) were caregivers of HIV positive children and the others were attending the clinics for their own treatment. Two hundred and forty-one (72.6%) answered that HIV infected children below 15 years should be informed about their status with appropriate age for disclosure as 12 years (IQR 10-15). Most answered that the status should be disclosed by biological parents (68.7%), followed by healthcare providers (17.8%). Over 80% answered that they were comfortable discussing the issues of HIV and sexuality with children. Those with higher education level (adjusted OR 1.89, 95%CI 1.02-3.50) and not being biological parents to the child (adjusted OR 3.44, 95%CI 1.01-11.73) were more likely to feel comfortable to talk compared to their counterparts. One hundred and forty-five (43.7%) agreed on adolescents’ access to HIV and family planning services without caregivers permission. Those who were not caregivers of the children were found to be more supportive for adolescents’ access to these services (adjusted OR 2.01, 95%CI 1.25-3.23).

Conclusions: In general people attending the ART clinic have positive attitudes towards adolescent HIV care services including sexual and reproductive health. This was more significant among those who were not biological parents or caregivers of children; their active involvement may be the key to further strengthen adolescent care.

No conflict of interest

Abstract: AB_03

HIV infection and adolescents

Reproductive Health Decision-Making in Perinatally HIV-Infected Adolescents and Young Adults

Introduction: Improved access to antiretroviral therapy in the United States and, increasingly, internationally has increased the survival of many perinatally HIV-infected (PHIV+) children who are living into adolescence and adulthood, becoming sexually active and making decisions about their reproductive health. The literature focusing on the reproductive decisions of individuals behaviorally infected with HIV can serve as a springboard for understanding the decision-making process of PHIV+ youth. Yet, there are many differences between the two populations. Given the potential public health implications associated with reproductive decisions, better understanding of factors influencing the decision-making process is needed to help inform the development of salient treatment and prevention interventions.

Materials & Methods: To begin addressing this understudied area, a ‘think tank’ session, comprised of 12 clinicians, medical providers, and researchers with expertise in the area of adolescent HIV, was held in Bethesda, MD, on September 21, 2011. Three primary goals were: 1) to explore what is known about factors that influence the reproductive decision-making (RDM) of PHIV+ adolescents and young adults, 2) determine what important data are needed in order to develop appropriate intervention for PHIV+ youth having children, and 3) recommend future research directions.

Results: The think tank participants recommended a developmental perspective be applied considering factors that may influence reproductive decisions, including the effects of...
early brain development, mental health outcomes, disclosure of HIV status to the patient/others, and health behaviors such as sexual behavior and substance use. Gaps in current knowledge regarding the role that psychosocial factors such as gender, family constellation, and loss may play in RDM were identified. Specific questions related to the medical management of PHIV+ adolescents included the risk for post-partum depression and levels of ART adherence during pregnancy. Additional questions were raised about the amount/nature of reproductive health information shared with PHIV+ adolescents, given that providers may not have expected their PHIV+ patients to survive into adulthood. Finally, participants stressed the importance of designing future studies with appropriate control groups, use of creative means to improve response rates such as social media or texting, and encouraged the application of self-efficacy to specific skills and behaviors.

Conclusions: Answers to the above-mentioned questions will have implications for policy and service delivery - particularly keeping risk reduction front and foremost. Youth growing up with HIV come from extremely high-risk backgrounds with associated mental health problems. However, they share more commonalities with their typically developing peers than not. They are future-oriented and many have a strong desire for having children. While it is not possible to address all the questions and suggestions for future research focused on maturing PHIV+ youth, the recommendations from the think tank provide suggestions for ways the field can move forward. There is an opportunity to help youth develop a healthy sense of sexuality, including decisions about reproductive health. Researchers, clinicians, and systems of care are strongly encouraged to keep pace with the emerging needs of this special population as their life spans continue to lengthen.

No conflict of interest

Abstract: AB_04

HIV infection and adolescents

Hyperproteinemia in children should lead to HIV testing

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Introduction: HIV infection is underdiagnosed in children, in all settings, although most of the children finally diagnosed with HIV had presented previously to health care facilities. A common biological finding in infected children is polyclonal hypergammaglobulinemia, which raises in turn the serum protein level. We decided to evaluate the potential usefulness of a simple marker, easily accessible in routine practice, the serum protein level.

Material and Methods: In one tertiary level pediatric hospital in Paris, we did a retrospective analysis of sociodemographic, clinical and laboratory data of children diagnosed with HIV infection between 2000 and 2010 including sex, age, country of origin, presenting signs, serum protein level, HIV viral load, CD4 cell count.

Results: Out of 83 children newly diagnosed protein levels were available before antiretroviral therapy was initiated for 52 children. 46 of 52 patients were of African origin (half of them recently arrived in France). The mean age was 5 years and 6 months (range 0 to 17 years); 35 were older than 2 years old (20 girls, 15 boys), 17 were under 2 years old (10 girls, 7 boys). Among the patients older than 2 years old, the mean level of serum protein was 96.3 g/L (70-127) and 32/35 patients (91%) had hyperproteinemia; the 3 patients with protein level in the normal range were two patients just over 2 years old and an adolescent with a recent sexual transmission. Among the less than 2 year-old, the mean level of serum protein was 77.9 g/L (59-122), with 9/17 patients (53%) having hyperproteinemia, according to the standards for age.

Conclusion: Hyperproteinemia is a common finding in HIV infected children, at levels often far
above normal values. It could be an helpful surrogate marker in resource constraint settings, to consider offering HIV testing.

No conflict of interest

Abstract: AB_05

HIV infection and adolescents

Situation of children and teens with HIV in Argentina: looking for gaps in the route towards universal access

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Introduction: Strategies implemented for prevention of mother to child HIV transmission have been highly effective in our country. However, opportune start of antiretroviral treatment in the first months of life and availability of adequate spaces for adolescents are pending challenges in this population.

Methods: To analyze information available through epidemiological surveillance and data provided by health institutions in order to identify gaps in the response for children and adolescents with HIV in Argentina

Results: Since the beginning of the epidemic through December 2010, 7941 cases of HIV infection in children under 19 years were reported, of which 58% are under 14 and 42% are teenagers under 19. Transmission routes are clearly differentiated, while 90% of those under age 14 were infected through perinatal transmission, adolescents were predominantly transmitted through unprotected sex. While the number of diagnoses in adolescents and young people aged 15 to 24 remains relatively constant over the years, those who are under 14 decreased over the decade. Half of the diagnoses in children under 14 years were recorded between 1990 and 2000, 44% of diagnoses in adolescents occurred in the last 10 years. These data are consistent with those of the central laboratories showing a drop of the seropositivity of children with perinatal exposition to HIV (since 13.7% in 2000 to 4.4% in 2009), but they also report 30% of uncompleted diagnosis. During the complete period, 40% of children, infected by perinatal transmission were diagnosed after the first year of life. More than 90% of children, who are under medical supervision, are receiving ARV therapy. Neither pediatric services nor infectology services for adults are accustomed to take care of adolescents infected by sexual transmission.

Conclusions: Despite successful reduction of vertical transmission, there is an high percentage of exposed children that do not complete the diagnosis process in our country. Coverage of ARV treatment demonstrates the consensus about the benefits of timely treatment in this population; however it is necessary to strengthen the pediatric diagnostic circuits to ensure early start of treatment in all infected children. On the other hand, the difficulty categorizing adolescents into pediatric or adult systems of care and the lack of access of many teenagers to medical services are obstacles in the road to universal access.

No conflict of interest

Abstract: AB_06

HIV infection and adolescents

What could we learned from sharing experiences within HIV adolescents? the case in resource-limited settings

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**Background:** Disclosure of HIV status to a child should put him at center of his health concerns and sharing experiences with peers remains a huge challenge especially in adolescents. This study aim to describe the challenges and benefits of HIV infected adolescents a camp retirement.

**Materials and Methods:** Prospectively followed adolescents at Care Unit for Children Exposed or Infected by HIV(CUCEIH-Centre of Excellence), Military Teaching Hospital, Benin were invited for sharing experiences during a so-called 'retirement camp' organized by OptimaBenin and Caritas. Methodology ‘of the memory box’ with qualitative approach using descriptive and interpretive phenomenology was applied to 2 groups of 20 adolescents (50% girls). Interactive participatory, in-depth interviews, focus groups, history reconstruction, ‘Memory Box’ development, letters to deceased parents/relatives, Life river, sociogenogram, heroes books, and entertainment were conducted for 10 days. Lodging was arranged considering their characters, sex and behavior. Selected HIV-adolescents were in high school, orphaned, informed of their status. Consent was obtained from them and their parents/caregivers. Camp Staff (2 psychologists, 3 social workers, 1 community worker) collected data using resilience questionnaires, feelings scale, recordings/films. After 12 months, this camp was evaluated during 2 days with qualitative approach using in-depth interviews and focus groups. Their opinion as well as what they really gained were assessed. Parents and health care professional was also involved. Ethics committee Approval was obtained, and informed consent was required from both children and parents.

**Results:** Sharing experience within adolescents is possible and very productive: they can describe and share their experiences, and resilient and able to begin prospects for their life. They now have great confidence in their future, have expressed their responsibility in their perception of HIV disease and treatment adherence. Knowing their status was a key motivation to make this camp a success. Their contribution to the model of care and their willingness to support this initiative was substantial. Challenges faced by organizers were consent obtained from parents/caregivers and management of psychological issues when remembering painful memories.

Moreover, 12-month evaluation showed that their resilience was reinforced in regards to their environment and financial and social difficulties. They drastically improved their relationship with their parents as being more able to take care of their health. Comprehensive reproductive health program was their utmost concern. Parents were so happy with these transformations of their child in regards to their behavior and school performance. Adolescents were engaged to serve as peer support as well as expressing their willingness to contribute to another retirement camp that could be organized for HIV adolescents.

**Conclusions:** Community support should integrate this capacity building activities as continuum of care, given the benefits obtained in terms of behavior changing(ownership, commitment) and hence contributing to better access to care for HIV adolescents.

No conflict of interest

**Abstract: AB_07**

**HIV infection and adolescents**

**Teen Leaders as Counselors at Camp Hope Botswana: A New Initiative in the Empowerment and Care of HIV-Positive Children and Adolescents in Botswana**

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**Background:** Botswana-Baylor Children's Clinical Centre of Excellence (BBCCCOE)'s annual Camp Hope is a weeklong camp for its most vulnerable young patients, providing them with a chance to normalize their social experiences and improve medication adherence. In 2011, Botswana-Baylor piloted the use of Gaborone teen leaders (10 peer-elected teens trained in leadership skills who help plan and facilitate Teen Club) as camp counsellors. As
leading Teen Club’s 150 teens proved challenging, this pilot aimed to increase the teen leaders’ confidence, self-esteem, leadership skills, and feelings of control over their own lives, ultimately paving the way for their healthy transition into adulthood, as well as their campers’ into adolescence.

Materials and Methods: Teen leaders were role models of good behaviour and commitment to zero-transmission lifestyles. All assisted with twice-daily antiretroviral therapy (ART) distribution to campers. Nightly meetings with BBCCCOE staff were held to discuss challenges and lessons learned.

Results: Teen leaders’ self-esteem and confidence grew visibly; self-doubt and insecurity faded as the week progressed and they excelled as leaders. At the following Teen Club, previously-timid teen leaders commanded attention and took responsibility for a smoothly run event.

Conclusions: Settings such as Camp Hope in which young leaders feel in control of and respected by their younger charges and are closely supported by supervisors is an effective and fun training ground for more challenging leadership positions. Feeling empowered and in control of their lives can lead to adoption and maintenance of healthy behaviors including good adherence and safe sex practices. Additionally, Camp enabled teen leaders to bonded, reducing feelings of loneliness and stigma as they were better able to voice their feelings and opinions in respectful, productive ways. Botswana-Baylor Teen Club will continue using teen leaders as Camp Hope counselors. In coming years, teen leaders will take ART with campers to model perfect adherence.

No conflict of interest

Abstract: AB_08

HIV infection and adolescents

Perspectives of HIV Infected Batswana Children on their Schooling Environment


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Background: Rollout of highly active antiretroviral therapy (HAART) means perinatally HIV-infected children are surviving into adulthood. However, there is a dearth of studies on children’s own views and perceptions to guide policies for this growing cohort.

Methods: A structured interviewer-administered questionnaire was used to collect data from a representative sample of children on HAART aged 6-18 years between August 2010 and February 2011. A total of 12 public HIV treatment clinics covering over 90% of all children receiving HAART in Botswana participated.

Results: Of 984 children surveyed 974 (99%) were in school; and 970/981 (98.9%) liked school. The children gave 1615 reasons for liking school: wanting to learn 1029 (63.7%), friends 173 (10.7%); sports 131(8.1%); opportunity to play with other children 127 (7.9%); and because of teacher 89 (5.5%). Despite generally liking school, 760 of 974 (78%) respondents indicated they faced problems in school such as: poor school grades (36.4%), health/illness/poor attendance (17.8%), inadequate scholastic materials (7.8%), negative interaction with other children (4.8%), lack of friends (4.7%), stigma (4.3%), and lack of money to pay school fees (3.7%). A total of 1256 responses were elicited from 973 children when they were asked to name two most important things that could be made better for them in school such as: extra learning support 176 (14%), improved school meals 144 (11.5%), protection from bullying/teasing/stigma 127 (11.1%), more scholastic materials 117 (9.3%), more leisure/entertainment/extracurricular activities 108 (8.6%), more love/patience by teachers 102 (8.1%), improved school infrastructure 101 (8.0%), and better teacher attendance/teaching approaches 58 (4.6%). Of 1179 responses from 970 children, 152 (13%) indicated they had no one to talk to in school who could help when they felt upset, sad or frustrated.
Conclusions: Children living with HIV are calling for the creation of an empowering, empathetic, supportive, caring, and non-discriminating school system.

No conflict of interest

Abstract: AB_09

HIV infection and adolescents

Stitch-by-Stitch: A Pilot Income-Generating Project (IGP) to Empower Teen Mothers at a Paediatric HIV Treatment Centre in Botswana

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Background: As HIV-infected children reach adolescence, they need to feel a sense of control and self-sufficiency. Options for achieving these are limited in Botswana, and economic determinants are clearly linked to sexual risk-taking by youth: intergenerational and transactional sex and the attendant consequences. However, few psychosocial support programs for HIV-infected teens incorporate IGPs as a means of empowerment. Stitch-by-Stitch targeted HIV-infected teen mothers who are also Botswana-Baylor Children’s Clinical Centre of Excellence (COE) patients, with the objective of improving their self-efficacy, future orientation and self-care, ultimately leading to better adherence and clinical outcomes for both mother and baby.

Methods: Pediatric AIDS Treatment for Africa (PATA) provided funds to design and sew 220 bags for PATA’s annual conference. BWP13,550.00 was paid to a local tailor to provide sewing machines and teach the teens professional-level sewing, BWP3,788.40 for teen transport and lunches, BWP10,553.30 for materials. Over 35 days, 8 hours Monday-Friday and 6 hours Saturdays, 10 teens worked with the tailor and COE staff-volunteers in a converted COE clinic room. Attendance was taken daily and teens wrote post-project assessments

Results: 220 bags were sewn at BWP150.00 each, with a final profit of BWP5,150.00 to be used to support future COE IGPs. Range of days worked per teen was 1-27, median 3.5, mean 7.6.

Conclusions: This is the first description of a successful IGP as a psychosocial support intervention, developed and operationalized in a low-resource clinic setting. Evaluations of teens’ experiences, including assessment of skills learned and future utilization, and follow-up of participants’ adherence and clinical outcomes would be of interest. Derivative benefits likely include developing senses of responsibility and self-efficacy, improving future outlook and understanding of the link between self-sufficiency, self-care, staying healthy and the importance of treatment adherence. Future IGPs at the COE will avail to all interested teens and include continuing Stitch-by-Stitch.

No conflict of interest

Abstract: AB_10

HIV infection and adolescents

Labour of Love: Caregivers' Self-Reported Challenges in Caring for HIV Infected Children

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Background: In general, the care of sick children is predominantly the responsibility of adult females who are already burdened with other demanding social, economic and household chores. This study investigated the challenges faced by caregivers of HIV-infected children in Botswana.
Methods: The study was conducted among primary caregivers of HIV-infected and affected children and adolescents, using a cross-sectional design, in 12 antiretroviral therapy sites accounting for over 90% of all HIV-infected children receiving Highly-Active Antiretroviral Therapy in Botswana. Data were gathered using interviewer administered questionnaires and focus group discussions. Quantitative data were analyzed using descriptive statistics. Qualitative data were grouped into mutually exclusive categories according to themes emerging from the data. Ethical approval was obtained from the Ministry of Education & Skills Development, the Ministry of Health's Health and Research Development Committee and Baylor College of Medicine's Institutional Review Board.

Results: About 92% of the caregivers for HIV infected children were females. The caregivers cited various challenges, including: being saddened by the realization that a child in their care was HIV positive; the difficulty of explaining why the child had to take daily medications at regular, pre-scheduled times; the difficulty of disclosing the positive HIV-status of the child to others; the fear that the child may not accept his/her HIV positive status; having to answer questions that follow the disclosure; being unable to adequately meet the needs of the HIV infected children; and the fear of testing HIV positive.

Conclusions: Caregivers face enormous and wide-ranging challenges in caring for the HIV infected children. Governments and non-governmental organizations should design systems and programs aimed at supporting and boosting the morale and well-being of caregivers of HIV infected children.

No conflict of interest

Abstract: AB_11

HIV infection and adolescents

O’icheke Campaign Year 1: Changing Attitudes and Behaviours Towards Multiple Concurrent Partnerships

Amongst HIV-Infected Adolescents in Botswana

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Background: MCP is a chief driver of HIV transmission in Botswana. In response, Botswana's National Prevention Operational Plan, funded by the World Bank and coordinated by the National AIDS Coordinating Agency, promoted a nationwide campaign (O’icheke) with MCP as year one’s focus. As the only implementing organization targeting HIV-positive adolescents, BBCCCOE Teen Club's objective was to evaluate and increase HIV-positive adolescents' knowledge and understanding of the link between MCP and the risk of contracting sexually transmitted infections including HIV, ultimately aiming to prevent new HIV infections and re-infections.

Methods: Using the Teen Club Model, educational sessions were held once a month in Francistown, Selebi-Phikwe, Goodhope, Southeast and Kweneng East. Teen Club life skills curricula were adapted and/or developed on stigma, discrimination and disclosure; gender equality; communication; medication adherence; confusion between traditional cultural practices, mutual monogamy, polygamy and MCP; and an essay-writing competition about challenges and opportunities of being an HIV-positive teen. Peer-elected Teen Club members helped design and implement events and enabled their peers to identify with material. Peer educators were trained to implement the campaign and counsel HIV-positive teens. Pre- and post-tests given at each session assessed teens' knowledge and attitudes about MCP-related topics.

Results: In year one, 13 peer educators were successfully trained, 90 life skills activities conducted, and 258 HIV-positive teens reached with MCP messages/related topics. Programme evaluations showed consistent improvement in teens after MCP sessions, with a pre-test mean score of 64% and post-test 81% across all sites. Qualitative feedback was also consistently positive.
Conclusions: Basic HIV knowledge amongst HIV-positive teens is poor; HIV education in schools and clinics needs substantial strengthening to improve clinical outcomes of HIV-positive youth. Next steps include addressing intergenerational and transactional sex via Teen Club’s life skills curriculum, development of new session topics and expanding our target group to adolescents’ broader support systems.

No conflict of interest

Abstract: AB_12

HIV infection and adolescents

O’icheke Year 2: Changing Attitudes Towards Multiple Concurrent Partnerships, Intergenerational and Transactional Sex Amongst Adolescents

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Background: To combat Botswana’s high HIV prevalence, the National Prevention Operational Plan began the nationwide O’icheke campaign in 2010. IG&TS emerged as drivers of MCP and became additional year two themes. After a successful year one, the World Bank and Botswana’s National AIDS Coordinating Agency funded Botswana-Baylor Teen Club for year two, aiming to prevent new HIV infections and re-infections by evaluating and improving knowledge, attitudes and practices (KAP) regarding MCP, IG&TS and HIV.

Methods: Still covering Francistown, Selebi Phikwe, Goodhope, Southeast and Kweneng East, BBCCCOE adapted and reinforced critical year one topics alongside year two’s themes: IG&TS, negotiation skills, the poverty-MCP link and income-generating activities. Previously-volunteer peer educators were hired as employees; teacher and caregiver training sessions were conducted. Impact surveys at year two’s end will evaluate change in teens and peer educators' KAP relating to MCP, IG&TS and HIV.

Results: Thus far, Teen Club attendance exceeds expectations; 5 hired peer educators were given more responsibility implementing life skills curricula and counselling HIV-positive teens; 60 life skills activities were successfully conducted for 256 HIV-positive teens; an ‘Empowerment Camp’ addressed gender issues for 49 teens; and 5 teacher and 5 caregiver trainings reached 86 teachers and 190 caregivers. Teacher trainings received exceptional feedback and prompted some teachers to become Teen Club volunteers.

Conclusions: KAP regarding HIV, MCP, and IG&TS are poor amongst HIV-positive teens and their support networks. O’icheke campaign year two reaffirmed that HIV education in schools and clinics needs strengthening if it is to increase the health and well-being of HIV-positive youth. In years three-four, Teen Club will expand to ten sites around Botswana, targeting 650 teens, their support networks and community leaders, and implement correct and consistent condom use and abstinence education. An assessment of Teen Club’s impact on participants’ KAP will be carried out at all sites.

No conflict of interest

Abstract: AB_13

Complications of HIV therapy

Determining Immune Reconstitution Syndrome in antiretroviral treated children in Indonesia

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Abstract: AB_14

Comprehensive Pediatric HIV care

Disclosure status of HIV-positive children receiving care at IeDEA-Central Africa clinics in Burundi, Cameroon, and the Democratic Republic of Congo

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Background: HIV status disclosure among children has not been widely assessed in sub-Saharan Africa where most HIV-infected children reside.

Materials & Methods: Data were obtained from 288 HIV-positive children aged 5-18 years receiving care at four HIV care and treatment clinics in Burundi, Cameroon and the Democratic Republic of Congo as part of the International Epidemiologic Databases to Evaluate AIDS (IeDEA) Central Africa region. We compared characteristics of those who knew their HIV serostatus (disclosed) with those that did not (undisclosed) using chi-square tests.

Results: Of the 142 disclosed children, 69% were between the ages of 5-11 years as compared to 75% of the 146 undisclosed children. Roughly half were girls (47% of disclosed, 50% of undisclosed). An equal proportion of both groups (55%) were enrolled in the IeDEA database at WHO clinical stage 3/4. 69% of disclosed and 60% of undisclosed children were receiving antiretroviral therapy (ART). Of 165 children for whom adherence data were available, few reported missing more than two days of ART (9% of disclosed, 12% of undisclosed). 82% of disclosed children and 51% of undisclosed children were on...
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cotrimoxazole prophylaxis (p< 0.05). 66% of disclosed children and 49% of undisclosed children were diagnosed through voluntary counseling and testing (p< 0.05) and only two through prevention of mother-to-child transmission programs. About half (42%) of disclosed children and 14% of undisclosed children attended a support group (p< 0.05). One-third (33%) of the 142 disclosed children learned of their serostatus between 5-11 years, 26% at 12+ years, and for 39 children, age of disclosure was unknown. The median age of disclosure was 10 years.

Conclusions: The majority of children did not know their HIV serostatus and were on ART though overall adherence was high. Disclosed children were more often on contrimoxazole prophylaxis and attended support groups than undisclosed children. Further inquiry is needed such as examining adherence over time and survival by disclosure status.

No conflict of interest

Abstract: AB_15

Comprehensive Pediatric HIV care

Growth patterns and health status of HIV-infected children living in an institutional facility in India

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Introduction: Orphanhood is a tragic consequence of the HIV epidemic worldwide and often compounds pre-existing malnutrition and ill-health among HIV-infected children. As the number of HIV orphans overwhelms the capacity of extended biological families to care for these children, a viable option is to provide institutionalized residential care for these children. Despite the high burden of pediatric HIV infection and adult deaths in India, there is a dearth of literature on the appropriate care of HIV-infected orphans in the country.

Materials & Methods: This study aimed to understand the health status of HIV orphans in a well-structured institutional facility in India using prospective longitudinal analysis of growth and anemia prevalence among these children. Sneha Care Home is a faith-based residential care facility for HIV-infected children hailing from an economically disadvantaged background, and who have lost one or both parents. The home takes on a 'holistic' approach with the children, thus attempting to provide care for the entire persona of each child, taking into account mental and social factors, rather than only physical and medical concerns. A prospective cohort study of all HIV-infected children residing at the Home between June 2008 and May 2011 for at least one year, was conducted. Clinical history, physical examination, anthropometry, dietary recall, CD4 and haemoglobin results were assessed. Statistical analysis included frequency distribution, chi square tests and non-parametric Friedman's test.

Results: Of the 85 children included in the study, mean age was 9.2 (range, 4-14) years and 60% were boys. Prevalence of anemia at entry into the home was 40%, with the cumulative incidence of anemia during the study period being 85%. At baseline, 79% were underweight and 72% were stunted. Children <7 years received 75% recommended daily allowance (RDA) for energy, while older children received 93-107% of RDA for energy. All children received adequate (>100% RDA) amounts of both protein and fat. Iron intake was low in all age groups, ranging from 38% to 69% of RDA. All children, irrespective of their ART status showed an improvement in nutritional status over time as demonstrated by a significant increase in weight (median weight-for-age Z score: -2.75 to -1.74, p<0.001) and height Z scores (median height-for-age Z score: -2.69 to -1.63, p<0.001). Pulmonary tuberculosis was seen in 8% (7/85) and other common infections included impetigo (31%), varicella zoster (24%), otitis media (15%) and parotitis (13%). A majority (75%) of these children had these infections in the initial period (of less than 3 months) of admission into the facility, and remained infection-free subsequently, underscoring the
role of health maintenance and good nutrition for preventing frequent intercurrent infections.

**Conclusions:** These findings suggest that good nutrition even in the absence of ART can bring about improvement in growth. The Sneha Care Home model is a feasible and replicable model that indicates that the holistic approach used in the Home may have been helpful in combating HIV, opportunistic infections and poor nutritional status in severely malnourished orphan children, and thus may contribute towards optimal management of HIV orphans globally.

*No conflict of interest*

**Abstract: AB_16**

**Comprehensive Pediatric HIV care**

**Delayed diagnosis of Pediatric HIV infection and impact on one year outcomes**

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**Introduction:** Large numbers of children are born outside organized maternal and child HIV care system in India. Only 50% of pregnancies in Surat City report HIV testing. Timely diagnosis of HIV infection in children is mainly dependent on provider initiated testing. Timing of diagnosis of HIV infection and its impact on outcomes in Indian children is not known.

**Material and Methods:** A prospective cohort study with one year follow-up was performed at New Civil Hospital, Surat, India, during 2008-2010. Surat is a large metropolitan city with a population of 4.7 million. Newly diagnosed HIV infected, antiretroviral naive children, 2 to 15 years of age, who could be followed up regularly during study period were eligible for inclusion. HIV infection was confirmed by HIV antibody based ELISA (Enzyme Linked Immuno Sorbant Assay) tests. Timing of diagnosis (early versus late) was assessed at baseline based on disease stage (WHO staging criteria). Disease stage and CD4% were documented at baseline, 6 and 12 months. Patients were followed monthly and provided standard care including antiretrovirals according to national guidelines.

**Results:** Of the 487 children screened for HIV based on clinical suspicion, 67 (14%) were confirmed positive. Of those 40 met the inclusion criteria; 55% (22/40) were males. 63% were above 5 years of age at the time of first diagnosis. Maternal seropositivity was confirmed in 75% of cases from past medical records of mother or voluntary testing. Maternal HIV status was unknown due to maternal death in 5%, separation in 12.5%, and refusal for testing in 7.5% of the cases.

At initial evaluation 50% of the HIV infected children met criteria for advanced stage of HIV disease (37.5% and 12.5% in WHO stage 3 and 4 respectively). Base line mean CD4% of stages 1, 2, 3 and 4 patients were 36%, 27%, 22.5% and 12.5% respectively. Over the first six months since diagnosis, clinical recovery (change in WHO staging) was observed in only 40% of stage 4 patients compared to 62.5% and 73% in stages 2 and 3 respectively. Only 1 of 12 patients in stage 1 progressed to stage 2 over the follow-up period. No deaths were reported in the cohort during the study period.

At 12 months, compared to baseline, mean CD4% increased by, 13.5%, 16% and 5% in stage 2,3 and 4 patients, respectively.

**Conclusion:** Diagnosis of HIV infection, even in cases of known maternal HIV disease, is delayed among children in this large metropolitan city of India, allowing disease progression to advanced stage. Clinical and immunological recovery is slow despite standard of care and interventions including antiretrovirals in patients diagnosed in late stage HIV disease. Our findings underscore the need for sensitizing healthcare providers about optimizing maternal and infant HIV testing and strengthening the linkage to care to prevent delays in diagnosis of HIV infection in children.

*No conflict of interest*
Abstract: AB_17

Comprehensive Pediatric HIV care

Tutoring Programme: Improving the School Performance of HIV-infected Children at the Botswana-Baylor Children's Clinical Centre of Excellence

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Background: Frequent school absenteeism due to illness and clinic visits, HIV-associated cognitive impairment, and high parental loss rate make school success difficult for HIV-positive youth. Poor school performance can lead to bleak future outlooks, helplessness and poor medication adherence. BBCCCOE's Tutoring Programme aims to evaluate and improve BBCCCOE patients' school performance.

Methods: In 2010, BBCCCOE initiated a free-of-charge Tutoring Programme based on Botswana's national education curriculum. 3-10 volunteers tutor patients from 9:00am-noon on Saturdays at the BBCCCOE, individually whenever possible. Academic materials were assembled for commonly requested topics in mathematics and science; books are available for in-session and at-home use. Tutors complete intake assessments for new tutees and evaluate students' progress post-sessions.

Results: 49 patients have been tutored, 29 attending >5 sessions. Students range from 11-21 years old (mean:15 years) and from Standard 1- Form 5, most commonly Standards 5(17%) and 6(15%). Most requested subjects are mathematics, science and agriculture. Tutors most commonly report problems with students' inability to read at grade level (18/49 tutees must 'go back to basics') and 'difficulty understanding key concepts, Mathematics and English.' Many students are at inappropriate grade levels for their age.

Conclusions: Initially for homework support, the Tutoring Programme evolved to meet the need for remedial education due to students' lack of fundamental knowledge. Ways forward include development of academic materials for more subjects such as reading comprehension, end-of-term assessments for all tutees and twice-yearly tutor training sessions, and encouragement of tutor-tutee mentoring relationships to boost program efficacy and students' self-confidence, interest in learning and ultimately school performance. Successfully operationalized at a paediatric HIV clinic in a low-resource setting without funding or costs to the clinic or participants, the Tutoring Programme is accessible to all and replicable in all settings.

No conflict of interest

Abstract: AB_18

Treatment of pediatric HIV infection

Pharmacy Factors, Adherence to Antiretroviral Therapy and Outcome in HIV-Infected Children and Adolescents

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Background: Adherence to antiretroviral therapy (ART) in children depends on a combination of multiple factors including parental and child involvement and steady access to antiretroviral (ARV) medications. This study was conducted to evaluate the relationship between pharmacy factors, self-reported adherence and the virologic outcome in children and adolescents with HIV.

Materials & Methods: This was a prospective cohort study of pediatric HIV-infected patients 1-18 years of age. Self-reported adherence and pharmacy factors were assessed through interactive recall questionnaire-based interviews by the clinic staff with the caregiver and older
children (>10 years of age) during routine clinical visits every 3 months. The HIV RNA viral load (VL) was obtained from medical charts. Univariate and multivariate analyses were used to evaluate the association between self-reported adherence and virologic suppression (HIV RNA <400 copies/mL).

Results: The study recruited 97 pediatric patients (47 male/ 50 female). The majority of the patients (66%; n=64) reported being adherent, while one third (34%; n=33) of patients reported being non-adherent. Self-reported adherence was a significant predictor of virologic suppression (OR=6.07, 95% CI=1.86, 19.77). There was no association between pharmacy refill method (home delivery vs. pharmacy pick-up) and self-reported adherence (p=0.74). The most common barrier for adherence was ‘forgetting to take medications’, accounting for 17.5% of all visits. Pharmacy related problems (lack of refills, delayed delivery, errors in refills) were the second most significant barrier for adherence reported in 13.9% of all visits.

Conclusion: Self-reported adherence was found to be a reliable predictor of virologic suppression in the cohort of pediatric and adolescent HIV-infected patients. Pharmacy related factors represented the second most significant barrier to ARV adherence after forgetfulness. Interventions aimed at establishing a system of reminders and resolving the pharmacy related delays/problems with ARV medications supply may be helpful in improving adherence to ARV among HIV-infected children and adolescents.

No conflict of interest

Abstract: AB_19

Treatment of pediatric HIV infection

Retrospective study of factors associated with ART failure in HIV infected children at Ambulatory Treatment Center in the city of Brazzaville, Congo.

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Background: Limited data exists regarding factors associated with first-line antiretroviral therapy (ART) failures in HIV infected children. Such data is important in ART program evaluations and quality improvement planning.

Methods: All children under 15 years of age at the time of ART initiation were enrolled in study. Social surveys of children are regularly assessed in the center. Lack family support was defined as children who had low or no assistance when taking theirs drugs. Treatment failure was defined according to WHO recommendations. Retrospective chart review among children in December 2011 with descriptive statistics and case-control analyses.

Results: 151 children had started ART [(53.6% F), mean age at ART initiation=6.8 years (range 0.5-14 years)] last 8 years, all were in Nevirapine or Efavirenz based regimen. 15 (9.9%) had switched to second line ART ([didanosine +abacavir]+ lopinavir/ritonavir). At time of second-line switch, 67% had CD4 counts< 100 cells/mm3, Viral load was checked to all of them and was>100000copies/ml in 60% of cases. The mean duration of therapy at time of ART switch to second line was 3.5 years (range 0.5-8 years). Children who failed first-line ART were more likely to be over 6 years of age compared to younger (OR=4.5; 95% CI=1.2-16.5). While not reaching statistical significance, data suggests those who failed first-line ART were more likely male sex (OR=1.8; 95% CI=0.6-5.3) and had lack of family support (OR=3.11; 95% CI=0.9-10.5). At month 6 of second line therapy, 11 children had undetectable viral load (<400 copy/ml), 3 had viral load>400copies/ml.

Conclusions: We found in children treated in our facility that the factors related to reduced response to initial ARV therapy included older age, male sex and lack of family support. Social Surveys should be assessed regularly during follow-up.

No conflict of interest
Abstract: **AB_20**

**Treatment of pediatric HIV infection**

**Age differences among HIV-positive children receiving care at IeDEA-Central Africa clinics in Cameroon, Burundi and the Democratic Republic of Congo**


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**Introduction:** The International Epidemiologic Databases to Evaluate AIDS (IeDEA) provides a unique opportunity to examine characteristics of children receiving HIV care by age in the central Africa region where availability of pediatric HIV data is limited.

**Material & Methods:** Data were obtained from 476 HIV-positive children receiving care at four HIV treatment programs in Cameroon, Burundi and the Democratic Republic of Congo at enrollment into the IeDEA Central Africa database and among 113 children on antiretroviral therapy (ART) at 6-12 months.

**Results:** Of 476 children, 165 were aged 0-59 months, 230 were 5-11 years, and 81 were 12+ years. The majority of children were male (51%), on cotrimoxazole prophylaxis (65%), and on ART (52%) at enrollment into the database. At enrollment, 69% of children 0-59 months, 50% of children 5-11 years, and 63% of children 12+ years were classified as WHO clinical stage 3/4 (p< 0.05). Of 155 children who had baseline CD4 results, the majority of children aged 0-59 months (64% of 39) and 12+ years (62% of 26) were classified as advanced/severe as per WHO severity of immunodeficiency guidelines as compared to one-third of children (34% of 90) aged 5-11 years (p< 0.05). Of 113 children on ART with 6-12-month follow-up data, 88% of children aged 0-59 months were classified as WHO clinical stage 3/4, 57% of children 5-11 years, and 65% of children 12+ years (p< 0.05). At 6-12 months, 12% reported missed doses of medication and 19% knew their HIV serostatus. Few children (N=8) had viral load results.

**Conclusions:** Children aged 5-11 years had less advanced HIV disease at baseline and follow-up as compared to children aged 0-59 months and 12+ years. Medication adherence was high despite low HIV serostatus disclosure. Few children had CD4 cell counts and viral load results highlighting the need for increased access to laboratory services in this region.

No conflict of interest

Abstract: **AB_21**

**Treatment of pediatric HIV infection**

**Growth patterns and body composition changes in pre-pubertal HIV-infected children in India**

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**Introduction:** Human immunodeficiency virus (HIV) infection is known to cause disturbances in growth and nutritional status along with alteration of body composition. Depletion of lean body mass can have a negative influence on HIV survival, particularly when underlying malnutrition is present. This study aimed to assess growth patterns and changes in body composition in pre-pubertal HIV-infected children in India.

**Material & Methods:** HIV-infected children aged 2-13 years were enrolled from two clinics (urban and rural), in South India in 2007-08 and
followed for 6 months. 24-hour dietary recall, anthropology and skinfold thickness were recorded. Weight-for-age (WAZ), height-for-age (HAZ) and Body mass index (BMI) Z-scores were based on CDC reference data. Body composition assessment included evaluation of fat mass (FM) and fat free mass or lean body mass (LBM) using Slaughter skinfold equations. Growth failure was defined as either underweight (<-2.0 WAZ) and/or stunting (<-2.0 HAZ). Statistical analysis included the use of frequency distribution, chi square, student’s t test, univariate and multivariate logistic regression analyses.

**Results:** Among 80 enrolled HIV-infected children, mean age was 7.4±3.0 yrs; 59% were males; 25% (20/80) had advanced clinical stage disease (CDC Clinical Stage B & C) and 36% were on antiretroviral therapy (ART) for >6 months (median, 19 months). The remaining 64% were clinically well with good CD4 counts and were not yet eligible to start ART as per National ART guidelines. Poor nutritional status was seen at baseline: 53% were anemic, and mean WAZ, HAZ and BMI Z score were -2.68, -2.21 and -1.64 respectively. Majority (69%, 55/80) of the children experienced growth failure. Children with mild disease (CDC stage N and A) had higher LBM than children with advanced stage (CDC stage B and C), (16.7kg vs 13.5kg; p=0.01). Compared to children with normal growth, those with growth failure had lower LBM (18.7kg vs 14.7kg, p=0.002). Children who were on ART at recruitment had higher LBM compared to those not on ART (18.5kg vs14.5kg, p<0.001). Independent predictors of high LBM were high energy and protein consumption, and presence of ART (r=0.8, p=0.001). Six months later, there was increase in WAZ (-2.68 to -1.93, p<0.001), HAZ (-2.21 to -1.67, p<0.001) and BMI Z (-1.64 to -1.23, p=0.54). The increase in LBM was greater among children on ART compared to those not on ART (18.5kg vs14.5kg, p<0.001). The increase in LBM was greater among children on ART compared to those not on ART; p=0.02. Additionally, over the time period of 6 months, LBM/Ht was found to decrease in children who were not on ART (-0.19gm/cm), while it increased in children who were on ART at baseline (+6.97gm/cm), and in children who were started on ART during the study period (+9.69gm/cm) (p=0.007).

**Conclusions:** Growth failure and loss of lean body mass was highly prevalent among Indian HIV-infected children. The role of diet rich in energy and protein is important for maintenance of LBM. The differential increase in LBM among those children on ART reiterates the role of ART in not only preventing loss of muscle mass, but also in increasing lean body mass, which is likely to improve survival of HIV-infected children.

*No conflict of interest*

**Abstract: AB_22**

**Treatment of pediatric HIV infection**

**Knowledge of HIV Transmission and Experience of Caregivers Administering ARVs to HIV infected Children**

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**Introduction:** Caregivers need to have adequate knowledge of HIV transmission to prevent spread of infection. They are also responsible for ensuring that HIV positive children on HAART in their care are not administered <95% of their medication for optimum therapeutic benefit.

**Materials & Methods:** This was a cross-sectional study carried out using questionnaires randomly administered in interview form to consenting 115 caregivers during clinic days. The 102 (88.7%) properly filled questionnaires were analysed using SPSS version 15.0

**Results:** Eighty-three (81.4%) of the caregivers were married, 88(86.3%) females, 94(92.1%) educated with a mean age of 36.54±10.41. More than half 56(54.9%) of the children were male, 91(89.2%) in school with a mean age of 6.98. Eighty-one (79.4%) of the children were on a fixed dose combination of AZT+3TC+NVP with 18(17.7%) were already on second line drugs. Eleven (10.8%) of the caregivers have disclosed HIV status to the child. Main reason for non-disclosure was the child was too young (90.8%). Caregivers’ knowledge of HIV transmission showed a high knowledge of transmission via blood transfusion (92.2%), breastfeeding (88.2%) average knowledge of transmission
through unprotected sex (56.9), use of unsterilized needles and sharps (57.8%) and below average knowledge of transmission through circumcision (40.2%), MTCT (35.5%) and via oral sex (12.1%). Most (93.1%) of the children take their medication willingly, in the cases (18.5%) where the children vomits 41% caregivers contacts the doctor for advice, 26% give the child another dose while 34% do nothing. Caregivers' know consequences of non-adherence to treatment can be that the child will get worse (83.3%), failure of medication (52.9) and children can develop resistance to the current combination of drugs (36.3%). Almost all (98%) the caregivers expressed various levels of satisfaction with current regimen.

**Conclusion:** There is need for intervention to improve caregivers' knowledge of HIV and its management in children on HAART.

**no conflict of interest**

**Abstract: AB_23**

**Treatment of pediatric HIV infection**

**An International Interlaboratory Control Program for TDM in pediatric HIV infection**

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**Background:** Therapeutic drug monitoring (TDM) can be useful in the management of HIV-infected children treated with antiretroviral therapy. The latest version of the DHHS pediatric guideline (November 2011) does not recommend TDM for routine use, but TDM can be beneficial in several clinical situations. A limited availability of certified laboratories to determine drug concentrations is mentioned as a limitation to perform pediatric TDM. The PENTA network (Paediatric European Network for Treatment of AIDS) has initiated a coordination-action to build laboratory capacity, called PENTA-LABNET. Within this project, a quality control (QC) program has been established among pharmacology laboratories that participate in PENTA studies. One of the goals of participation is the improvement of performance of analytical methods for antiretroviral drugs. Here we present the first results of this PENTA-LABNET program, as well as the outcome of a questionnaire among laboratories, participating in an international control program.

**Materials & Methods:** The PENTA-LABNET program is part of the International Interlaboratory Control Program for TDM in HIV infection (KKGT program), organized by the Dutch association for quality assessment in TDM and clinical toxicology (KKGT). Participating laboratories are asked to determine the antiretroviral plasma drug concentrations in several samples sent by the QC-program. Labs report the results of the blinded samples twice a year. Antiretroviral drugs assessed in the program included amprenavir, atazanavir (ATV), darunavir (DRV), efavirenz (EFV), etravirine, indinavir, lopinavir (LPV), nelfinavir, nevirapine (NVP), ritonavir, raltegravir, saquinavir and tipranavir. Here we focus on ATV, DRV, EFV, LPV and NVP. For the PENTA laboratories, the results were collected from 2009 to 2011. Next to the PENTA-LABNET program, all participants of the KKGT program were asked to fill in a questionnaire on TDM in children. For the laboratories performing TDM in children, the results of 2011 were analyzed.

**Results:** Seven PENTA laboratories participated in the PENTA-LABNET program. Results were reported for ATV, EFV, LPV and NVP by 5, 6 and 7 laboratories in 2009, 2010 and 2011, respectively, and for DRV by 4, 5 and 6 laboratories. The number of laboratories certified in 2009, 2010 and 2011, for ATV measurement were 3, 6 and 5; for DRV 4, 4 and 4; for EFV 3, 5 and 5; for LPV 5, 6 and 7 and for NVP 4, 6 and 6, respectively. Twenty-three of 47 participants of the KKGT program returned the questionnaire, and 15 of them reported analyzing antiretrovirals for children. Using anonymous codes, the results of 13 of these labs from the 2011 program were added to the results of the PENTA laboratories. Of these 20 laboratories, 15 (75%), 11 (55%), 15 (75%), 18 (90%) and 18 (90%) laboratories were certified for the analysis of ATV, DRV, EFV, LPV and NVP, respectively.
Conclusions: The PENTA-LABNET project resulted in more PENTA network laboratories certified for the analysis of antiretrovirals used in children. Among the laboratories participating in the KKGT program a high percentage of laboratories was certified for analysis of antiretrovirals commonly used in children. Most problems with the analysis were seen for measurement of DRV.

No conflict of interest

Abstract: AB_24

Treatment of pediatric HIV infection

Survival and Outcome of HIV-Infected Children after Antiretroviral Therapy in Malaysia

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Introduction: Malaysia is one of the countries with the fastest growing AIDS epidemics in East Asia and Pacific region. Paediatrics HIV constitutes around 1% of the positive cases. The objectives of this study are to evaluate the survival, the probability of achieving immunologic recovery and to examine factors associated with mortality among these children in HIV-infected children in Malaysia after receiving HAART.

Patients and Methods: Retrospective and prospective data collected through March 2009 from children in 4 different states in Malaysia enrolled in TREAT Asia’s Pediatric HIV Observational Database were analysed.

Results: Of 347 children in the cohort, only 278 (80.1%) were commenced on ART. The median duration of follow-up was 3.7 years with 32 deaths giving a crude mortality rate of 2.86 per 100 child-years. The mortality rate was highest in the first 6 months of ART was 10.62 per 100 child-years and declined to 1.83 per 100 child-years thereafter. The cause of death recorded for all 32 children were mostly related to infection: sepsis (n=12) pneumonia of any cause (n=7), encephalitis (n=3), tuberculosis (n=2), diarrhoea (n=2), and 1 each from malnutrition, cardiomyopathy, mycobacterium avium, rhabdomyosarcoma, lymphoma and progressive multifocal leukoencephalopathy. Age at commencement of HAART (< 0.001), baseline CD4% (< 0.001), baseline viral load (<0.042), and baseline weight for age z-score (< 0.015) were important determinates of immune recovery at 12 months after initiation of ART in this cohort. Low CD4 percentage, wasting (low weight for age z-score and height for age z-score), and anaemia at baseline were associated with mortality.

Conclusion: Children commenced on ART had high risk mortality in the first 6 months especially in those with low CD4 percentage, wasting and anaemia. Most death was associated with infection. These data support the need for early diagnosis and initiation of ART to improve survival.

No conflict of interest

Abstract: AB_25

Treatment of pediatric HIV infection

Adherence to antiretroviral therapy in HIV-infected children less than five years in Abidjan, Côte d'Ivoire and Ouagadougou, Burkina Faso


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Background: We measured the four days adherence to antiretroviral therapy (ART) and determined factors associated with a very high adherence in HIV infected children less than five years, followed in pediatric health care programs in Abidjan, Côte d'Ivoire and Ouagadougou, Burkina Faso.

Methods: We conducted a cross-sectional quantitative study in the clinical pediatric HIV care centers during the pre-implementation phase of the Monod ANRS 12206 trial from March to August 2011. All consenting caregivers (fathers, mothers, or guardians) of HIV-infected children less than five years on ART and followed at pediatric health care centers were consecutively interviewed on their attitudes, knowledge and practices about the pediatric taken ART. Adherence was defined as the proportion of doses reported by caregivers, taken by children compared to the prescribed doses in the last four days preceding the interview. Factors associated with a very good adherence (> 95%) were investigated by logistic regression.

Results: A total of 97 pairs of parents and children were included in the study (69 in Ouagadougou, 28 in Abidjan). Children’s median age was 3.4 years [IQR: 2.1 to 4.7]. Their median duration of pediatric ART was 15 months [IQR: 6 - 26]. ART was usually given to the child by her/his mother alone (80%), father alone (4%), either parents (3%), or others (12%). Close to 45% of caregivers knew writing, 77% had to manage another ART in the family, and 78% of fathers were aware of the HIV status of their child. According to caregiver reports, 89% had an adherence greater than 95%, 4% an adherence between 80% and 95%, and only 7% less than 80% adherence. These reported estimates were in agreement to the prescribed doses for 75% of the children, but underestimated for 13.4% children or overestimated for 11.3%. Child’s acceptation of ART administration was the main factor significantly associated with adherence > 95% (aOR: 5.1, 95% CI: 1.1-25.1, p = 0.04) adjusting for other factors (hours of drugs taken, antiretroviral prophylaxis during pregnancy and at birth, caregivers’ ability to write).

Conclusion: Under the field conditions in West Africa, the pediatric adherence to ART before five years old looks good in this child age group. Child acceptance of the ART administration and taste are crucial in improving adherence.

No conflict of interest

Abstract: AB_26

Treatment of pediatric HIV infection

WHO 2010 recommendations implementation in Benin for early treatment: what are benefits and challenges at paediatric site level?

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Background: To evaluate impact and challenges of WHO 2010 recommendations on paediatric ART site performance

Materials and Methods: Following adoption of WHO recommendations by Benin NACP, Care Unit for Children Exposed or Infected by HIV(CUCEIH-Centre of Excellence) at the Military Teaching Hospital, Benin drew an implementation plan consisting of ownership, constraints and operational analysis and Paediatric Cohort review to find children eligible to HAART. Performance indicators of paediatric HIV program (retention in the cohort, ARV treatment and mortality at 6 months) were compared between Group A (two years before the recommendations) and Group B (from January 2010 to October 2011). Age was divided into two categories and the Chi2 test used to compare proportions.
**Results:** Between 2008 and 2011, 196 infected children were recruited, Group B (n=91); female (54%), Less than 2 years (30%), clinical stage 3 and 4 (27%), HAART at admission (47%), mortality at 6 months (9%). Cohort review in January 2010 showed that 13 of 25 children <2 years not receiving HAART were eligible. Compared to group A, there was no significant difference for age, clinical stage and immunological category. Programme performance was better in Group B: eligibility at admission (58% vs 33%, p = 0.00), HAART within 1st months (62% vs 37%, p = 0.00), loss-to-follow-up (8% vs 20%, p = 0.00) and mortality at 6 months (3% vs 12%, p = 0.00). Difference between two groups was due to early access to treatment in children <2 years in Group B: Eligibility at admission in children <2 years was better in Group B (100% vs 20%, p = 0.00), while no difference was found for children more than 2 years (42% vs 38%, p = 0.68), the same for mortality (4% vs 31%, p=0.00) and (4% vs 6%, NS) respectively.

**Conclusion:** WHO2010 recommendations have positive impact on mortality and cohort indicators, especially for children <2 years. Leadership and management at paediatric site level is a key for implementation’s performance.

No conflict of interest

**Abstract: AB_27**

**Treatment of pediatric HIV infection**

**Effectiveness of first-line highly active antiretroviral therapy among HIV-1-infected children in South India**

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**Background:** Widespread access to ART in children has improved survival, but there are few studies on the effectiveness of ART, particularly among children using weight-stratified formulations of pediatric fixed-dose combinations (FDCs) that are in use in India within the national AIDS control program.

**Materials and Methods:** This is a cross-sectional analysis of treatment response among 80 HIV-infected children on first-line ART who were attending the pediatric infectious disease clinic at St. John’s Hospital, in Bangalore, India between 2009 and 2011. Viral load was measured using Abbott RealTime. Drug resistance genotyping was performed using an in-house method on those with viral load >1000 copies/ml, and interpreted using the Stanford database and the Tibotec Etravirine Weighted Genotype Score.

**Results:** All children were clinically asymptomatic. Virological suppression was seen in 85% (68/80) of these children with a mean duration of 26 months of therapy. Among the 12 children who were in virological failure, only two manifested immunological failure, only two manifested immunological failure (mean CD4 count, 26%±8). All of the children harboured subtype C viruses. Drug resistance genotyping identified M184V (n=11) as the most common NRTI mutation, and K103N/R (n=8), Y181C (n=4) and G190A (n=2) as NNRTI mutations. Etravirine cross-resistance was found in 5 children. No protease inhibitor (PI)-associated resistance mutations were seen.

**Conclusions:** A relatively high proportion of children on pediatric fixed-dose combination ART were responding well to therapy. The presence of drug resistance among those with no evidence of immunological or clinical failure highlights the need for periodic virological monitoring of children on ART in order to optimise treatment success and preserve future treatment options.

No conflict of interest

**Abstract: AB_28**

**Treatment of pediatric HIV infection**

**Frequency of drug resistance-associated mutations among HIV vertically infected children in Mexico**

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Background: Highly active antiretroviral therapy has increased survival rates in children with perinatally acquired HIV, with increased virological resistance and other consequences of extended antiretroviral use. The pattern of mutation frequency has been described in few studies in our country. This study evaluated the genotypic profile of HIV-1 isolates from treated (drug experienced and naïve) in Mexico. The prevalence of mutations in reverse transcriptase (RT) and protease (PR) genes were assessed.

Methods: Since June 2010 from September 2011, a multicentric cross-sectional study was conducted among HIV-infected children and adolescents (< 18 years) ARV naïve or drug-experienced, who had completed >6 months of ARV treatment, with virological failure, clinical and antiretroviral therapy data were collected. Genotyping was performed using Kit Viroseq HIV-1. ARV resistance mutations were analyzed in the Stanford HIV Drug Resistance.

Results: We evaluated 100 children and adolescents, 100% were infected with HIV perinatally; 40% were female, median age 8.2 yrs and median duration of ART at the time of the survey was 58.7 months (range 6-200 months). Viral load 178,333 cp/mL (41-2970713) and CD4+ count 684 (3-1741) at enrollment. We included four groups: 1) naive (18.6%), 2) patients in the first scheme (41.3%), 3) second and third scheme (18.6%) and 4) four or more schemes (18.6%). The frequency of resistance in the four groups for NRTIs, NNTR and PI respectively was as follows: group 1) 23.7%, 0%, 0%, group 2) 67.7%, 25%, 32.2%, group 3) 73.3%, 26.6%, 66.6%, group 4) 71.4%, 28.5%, 71.4%. We found > 2 TAMS by 7.6%, 12.9%, 6.6% and 21.4% of the 4 groups, respectively. A frequency of resistance to the three groups of ARV was found in 35% of patients with four or more regimens. The most frequent mutations were M184V (33.3%), conferring resistance to lamivudine and emtricitabina; thymidine-analogues amino acid mutations included: M41L (14%), T215Y (10.6%), L210W (5.3%) y D67N (5.3%). The most frequent NNRTI mutations were: K103N (13.3%), V108I (2.6%), Y188L (2.6%), Y181C (2.6%). The most common PI mutations were: M46I (14%), L10I (18.6%) y L90M (13.3%). All patients had HIV-1 subtype B, except one who had CRF02 AC subtype.

Conclusions: We found a high prevalence of drug resistance among children who received long term ARV. Development of strategies are urgently needed to limit the emergence of resistance.

No conflict of interest

Abstract: AB_29

Treatment of pediatric HIV infection

17 year followup of 10 recipients of an Autologous Therapeutic HIV Vaccine.

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An autogenous HIV/Cellular vaccine was administered to 10 HIV infected patients over a 48 week period in 1995. After 46 doses, no local or systematic adverse reactions were observed and laboratory studies for hematological, autoimmune and organ toxic events showed no significant change from baseline. Follow-up on this cohort occurred yearly for the first five years with subsequent follow-up in 2005 and 2011. After the first five years, there was no progression of HIV disease status and the cohort demonstrated clinical and objective laboratory evidence of disease stabilization and improvement. At the last visit in 2011, 9 of the 10 patients have survived with one death due to a motor vehicle accident. One individual had deterioration from progression of PML that was present at the time of immunization but never the less has two uninfected healthy children. The 8
remaining vaccine recipients have grown and developed to normal adults with negative or low viral loads with normal stable CD4 counts. The survival rate of this vaccinated cohort of 10 patients receiving the standard of care for HIV infection at the former Children’s Hospital AIDS Program (CHAP) in 1995, when compared to the survival rate of their age matched unvaccinated HIV infected cohort also receiving the standard of care showed a significant survival advantage. At this last visit in 2011, blood specimens were obtained and sent to the Human Vaccine Institute at Duke University for current state of the art humoral, cytokine and CD8/CD4 interactions that have come to define elite controllers with the expectation that this data will be available for inclusion at the time of the meeting. Elite Controllers are models for achieving functional cure with initial control of virus replication and viral set point important determinants of subsequent disease outcome. Understanding the mechanisms that allow elite controllers to maintain undetectable viremia over a long period of time would help to develop strategies for a functional cure for HIV infection. Establishing the correlates of immune protection for an effective Therapeutic HIV vaccines, are a viable option that would augment current drug regimens as well as have the potential to cure perinatal HIV infected infants, children and our currently aging up long term surviving adolescents. Taken together, there is now clinical and laboratory evidence supporting the use of an autogenous therapeutic vaccine. Innovative immune based adjuvant therapies including unique therapeutic vaccination, which would enable HIV infected populations to decrease their reliance on highly active antiretroviral therapies (HAART), lessening the side effects of these harsh medications, as well as enabling the areas of the world which find HAART drugs in short supply to confront the epidemic.

No conflict of interest

Abstract: AB_30

Treatment of pediatric HIV infection

HIV-1 drug resistance in a pediatric cohort under haart in decentralized setting in Senegal

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Background: Antiretroviral therapy in HIV infected children is frequently associated to virological failure and emergence of drug resistance. This cross sectional study aimed to determine the frequency of virological failure and to assess the prevalence of drug resistance mutations in children and young adults in a pediatric cohort in the suburb of Dakar (Senegal) after at least six months of HAART.

Material & Methods: Out of 126 HIV-1 infected children and young adults followed up in Roi Baudouin Hospital, 59 patients who were under first line therapy (2 NRTI + 1 NNRTI) for at least 6 month were included after their inform consent. Plasma viral load was determined using NucliSENS EasyQ v2.1 assay. Drug resistance testing was performed in case of virological failure with plasma viral load up to 1000 copies/ml (3 log copies/ml) by direct sequencing of full-length protease gene and partial reverse transcriptase using the in house ANRS technology. Drug resistance mutations were assessed by reference to HIVdb program V6.1.1 of Stanford University and the HIV French resistance algorithm V21. Subtyping was done by phylogenetic analysis using Neighboring method with ClustalX and recombinants were identified by similarity and bootstrap plots using Simplot V2.6.

Results: The study population was composed by 42 children with a median age of 11 years (ranging from 1 to 15) and 17 young adults with a median age of 17 years (ranging from 16 to 23) and the sex-ratio was 0.97. The median of CD4 count was 587 cells/mm3 ranging from 5 to 2000 cells/mm3.
Plasma viral load was detectable for 38 (64.4%) and 31 (52.54%) had a virological failure with more than 3 log_{10} copies/ml.
Genotyping was performed for 26 patients and showed the presence of drug resistance mutations in 96% of cases (n=25) giving 42.37% (25/59) of global resistance rate after 52 months of median follow up. Among these 25, mutations conferring resistance to NRTIs or NNRTIs were found respectively in 80% (n=20) and 100%. The most prevalent mutations were M184V (n=18), K103N (n=16), TAMs (n=11 including 8 T215YF) and Y181C (n=7). For NNRTI, an accumulation of drug resistance mutations was also noted with 17 strains harbouring more than one mutation and 3 presenting resistance to the NNRTI second generation Etravirine.
Genetic subtype distribution showed the predominance of subtype CRF02_AG (20/26, 76.92%) followed by 3 subtype C (11.54%) and 3 unique recombinant forms (11.54%).

Conclusions: High rate (52.54%) of virological failure was demonstrated in Senegalese children and young adults under first-line HAART with 42.37% of global resistance rate after 52 months of median follow up. These findings point out the difficulties of optimizing ART in children living in Sub-Saharan Africa, and the crucial need of laboratory monitoring reinforcement.

No conflict of interest

Abstract: AB_31

Treatment of pediatric HIV infection

Correlation between pill count adherence and virologic outcomes among children on salvage antiretroviral therapy in Botswana

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Background: Particularly in resource-limited settings, children and adolescents on salvage ART are at high-risk of losing future ART options; their adherence to salvage ART is a crucial concern. In settings where viral load(VL) determinations are available, assessing the effectiveness of ART is reasonably straightforward. For other settings, surrogate measures which predict ART effectiveness are of interest. Barring drug malabsorption or pharmacokinetic interactions, in the absence of antiretroviral resistance, excellent ART adherence should result in effective treatment. Settings, then, where salvage ART composition is based on the results of genotypic resistance assays, such as Botswana, provide an opportunity to evaluate this hypothesis and offer guidance which may assist less-resourced settings. This study assesses the correlation between pill counts and HIV VL among patients on salvage therapy at the Botswana-Baylor Children’s Clinical Centre of Excellence (COE).

Methods: Retrospective chart review of visits through December 2011 of all patients at the COE initiated on salvage ART, defined as lines of ART beyond Botswana's standard second-line ART of two nucleoside-reverse transcriptase inhibitors+lopinavir/ritonavir from January-December 2010. The poorest individual antiretroviral pill count adherence at each visit was noted and compared to the corresponding or nearest-available VL result.

Results: Of the 26 patients on salvage therapy, 17 (65%) were able to maintain pill counts between 95% and 105% on at least 9 occasions during the study period. However, only 5 (19%) were able to maintain an undetectable VL on a minimum of 3 occasions during the study period.

Conclusions: While an attractive potential predictor of ART effectiveness, in our setting there is a lack of correlation between pill counts and virologic suppression. Whether this is due to pill counts' susceptibility to manipulation by patients - a problem especially noted for adolescent patients - deserves further study. Children and adolescents merit very close supervision and objective measures of ART effectiveness.

No conflict of interest
Abstract: AB_32

Treatment of pediatric HIV infection

Clinical Variables Associated with Short Stature in HIV-infected children attending Botswana-Baylor Children’s Clinical Centre of Excellence

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Background: While it is well-established that HIV-infection is associated with growth failure in children, the clinical variables associated with short stature amongst HIV-infected children in Botswana have not been reported to date. The aim of this study was to assess in a population of HIV-infected children the association between short stature and clinical variables relevant to HIV viral load, CD4 count, adherence, whether the child is taking antiretroviral treatment (ART) or not, and adherence to ART.

Materials and Methods: Data was obtained by retrospective review of the electronic medical records of all patients attending the COE. Patients were grouped into categories: WHO-immunologic category (CD4 count/%), viral load, age(1-18 years), gender, degree of adherence(pill count), height, and ART yes/no. For each category the proportion of patients with height-for-age Z score (HAZ) score< -2 SD and < -3 SD was determined using WHO anthro/anthroplus software. Short stature was defined as HAZ< -2SD and profound short stature was defined as HAZ< -3SD. The Epimax table calculator was used to determine the statistical differences between the groups. p-value< 0.05 was considered statistically significant.

Results: Profound short stature(< -3SD) is more likely with severe immunosuppression (CD4%< 15%) than when CD4%>15%(OR:3.30, CI:1.51-7.09, p=0.002). Stunting is more likely with males than with females (OR:1.49, CI:1.19-1.87, p=0.001). Profound short stature is more likely with virologic failure(VL>400) than when VL is suppressed (VL< 400)(OR 2.64, CI 1.27-5.38, p=0.008) and when adherence is poor (< 95%) than when it is good (95-105%)(OR 1.72, CI 1.03-2.05, p=0.037).

Conclusions: In this cohort of HIV-infected children, profound short stature is associated with poor ART adherence, severe immunosuppression and virologic failure. Timely ART initiation and support in maintaining ART adherence are important interventions in supporting the growth of HIV-infected children. Our findings call for further studies into causal relations between these clinical variables and short stature, as well as future therapeutic interventions beyond ART.

No conflict of interest

Abstract: AB_33

Prevention of Mother-to-Child transmission

Adherence to antiretroviral prophylaxis during early infancy: The NISDI Longitudinal Study in Latin American Countries (LILAC) Study

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Background: Antiretroviral (ARV) prophylaxis is an efficacious intervention for preventing mother-
to-child transmission of HIV. We describe adherence to ARV prophylaxis reported by mothers or caregivers of HIV-exposed but uninfected infants enrolled in the NISDI LILAC protocol.

Methods: In 2008-2009, 401 HIV-infected, pregnant women were enrolled in a prospective cohort study (NISDI LILAC) at 12 sites in Latin America with access to infant ARV prophylaxis and replacement feeding. Infants were enrolled at birth, with follow-up at 6-12 weeks. Singleton, HIV-uninfected infants with at least one adherence report were eligible for inclusion in this analysis. The primary caregiver was interviewed at each visit regarding infant adherence to ARVs during the previous three days; percent adherence was calculated as total doses taken as a proportion of total expected doses. Adherence also was assessed as the last time an ARV dose was missed, and reasons for lack of adherence were ascertained.

Results: At enrollment, 99% of infants were receiving zidovudine alone. Adherence was calculated for 285 (78.9%) of 361 eligible infants at enrollment [282 (98.9%) had perfect adherence] and for 89 infants at the 6-12 week visit [84 (94.4%) had perfect adherence]. At the 6-12 week visit, caregivers of eight infants (9.0%) reported the last dose missed of any ARV was within the previous two weeks, four (4.5%) within the previous month, and two (2.2%) over a month ago. The remaining 75 (84.3%) reported no missed doses. Reasons cited for non-adherence included: did not want to awaken the infant, forgot, did not want others to notice him/her giving the ARV(s), and misunderstood the prescription.

Conclusion: High levels of adherence to infant ARV prophylaxis were observed. Reasons reported for non-adherence included not understanding the importance of administering ARV prophylaxis and concerns regarding disclosure of HIV infection status, both amenable to targeted interventions.

No conflict of interest

Abstract: AB_34

Prevention of Mother-to-Child transmission

Breastfeeding issues in regard to the 2010 WHO infant feeding recommendation at the PMTCT program in Mulago Hospital, Kampala, Uganda.

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Introduction: The 2010 World Health Organization’s (WHO) recommendation on infant feeding recommends Exclusive Breastfeeding (EBF) with an antiretroviral treatment intervention for the first six months of a child’s life to reduce transmission, and continued breastfeeding – with complementary feeding – until the child is at least a year old. The recommendation is based on recent literature demonstrating increased risk of infant and under two year mortality for HIV exposed uninfected infants whose mothers ceased breast feeding at 6 months. Despite the recommendation, it is still hard to overcome cultural norms which may include EBF for only about 6 weeks, followed by early introduction of other liquids or foods in resource limited settings. A qualitative formative research was carried out at Mulago National Referral Hospital to identify concerns, factors and attitudes which could affect uptake of the 2010 WHO recommendation.

Method: From September - November 2011, a qualitative formative research was carried out with different PMTCT stake holders to assess breastfeeding issues in regard to the new 2010 WHO infant feeding recommendation. The thematic areas of interest included; concerns, attitudes and factors likely to affect the uptake of the recommendation, length of breastfeeding among HIV-infected lactating mothers and influence on EBF. Five different Focus Group
Discussions (FGDs) were conducted with HIV-infected pregnant women (9), HIV-infected postpartum women (10), HIV-infected peer mothers (10), family members (10) and male partners (10) making a total of 49 participants. 12 key informant interviews were held with health care workers involved in PMTCT program and policy makers. All interviews were recorded, transcribed verbatim and coded for thematic and content analyses.

Results: 37 (76%) FGD participants and 12 (100%) Key Informants (KIs) responded to the theme on EBF for six months. The findings showed that, 57% FGD respondents and 100% of the KIs supported EBF for six months. Male partners were however unanimously unsupportive of the EBF for six months with fear of infecting the baby. 22 (45%) FGD participants and 12 (100%) responded to the theme on introduction of complementary feeds at six months with continued breast feeding. 75% of health workers supported the theme -- versus 36% of FGD respondents. 55% of the FGD respondents were unsupportive and majority feared baby getting wounds in the mouth thus increased exposure to HIV. 36 (74%) FGD participants and 12 (100%) KIs responded to who should take medicine between the mother and baby during breastfeeding. 89% FGD respondents favored mother and 11% both. Among the KIs, 58% favored mother, 17% baby and 25% both. 39 (80%) FGD participants responded to the theme on length of breastfeeding in HIV-infected mothers. Six months and above was supported by 41% and below six months by 36%. 26 (53%) FGD participants responded to the theme on who influences breastfeeding. 50% said health workers, 27% mother and 19% male partners.

Conclusion: Overall, the 2010 WHO infant feeding recommendation is likely to be supported by health workers and HIV-infected women but more sensitization should be targeted to the male partners to improve its support at the household level.

No conflict of interest

Abstract: AB_35
Prevention of Mother-to-Child transmission
Assessing gaps in PMTCT programming towards elimination of new HIV infections in children: A rapid assessment of the Zimbabwe national PMTCT program

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Background: The Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) has supported the national PMTCT program in Zimbabwe since 2001. By September 2010, over 834,000 pregnant women had received PMTCT services at 812 EGPAF-supported facilities in 38 of country’s 62 districts. At the end of 2010, EGPAF secured funding to support national expansion of the PMTCT program towards elimination of new pediatric HIV infections by 2015 using the 2010 WHO PMTCT guidelines (option A) as a catalyst. A national baseline assessment of the PMTCT program was conducted to inform this nationwide expansion.

Materials & Methods: A cross-sectional situation assessment was conducted between May and July 2011 at 1,317 health facilities in 59 of 63 districts in the country. A pre-tested questionnaire was interviewer administered to health facility management and service providers. This tool collected data on PMTCT services provided and gaps. Data were analysed using SPSS v 15.0

Results: Although most facilities 1245 (94.5%) were offering HIV testing and counselling (HTC) for PMTCT, only 9% were offering PMTCT according to the adapted 2010 WHO guidelines. The majority (65%) still followed 2006 WHO PMTCT guidelines while the rest (26%) were referring clients to the higher level facilities for ARV prophylaxis. Other gaps identified included:
limited ART eligibility assessment for pregnant women (with 50% of facilities performing WHO clinical staging, 7% with on-site CD4 testing), 14% initiating ART for pregnant women and lack of ART integration in PMTCT. Only 18.7% had mechanisms for mother-baby pair follow-up and only 44% were providing early infant diagnosis (EID) services.

**Conclusion:** Although the national PMTCT program has registered many achievements since its inception in 1999, there were several gaps to be addressed to achieve elimination of new HIV infections in children by 2015. Findings from this assessment informed the national- and district-level planning and the roll-out for implementation of the 2010 WHO guidelines in Zimbabwe.

*No conflict of interest*

**Abstract: AB_36**

*Prevention of Mother-to-Child transmission*

**Reasons of failure to prevent mother-to-child transmission of HIV among Russian women.**

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**Background:** The rates of mother-to-child transmission (MTCT) of HIV are higher (2.8%) in St. Petersburg as compared to Western European cities. The aim of this study was to evaluate the reasons of failure of the prevention of MTCT (PMTCT) among Russian women referred to a large HIV/AIDS clinical center in St. Petersburg.

**Methods:** The study prospectively analyzed the clinical characteristics (maternal age, history of intravenous drug use (IDU), co-infections, time of HIV diagnosis, use of antiretroviral prophylaxis (ARP), HIV viral load (VL)) of mother/infant pairs with MTCT. Descriptive statistics were used.

**Results:** MTCT occurred in 23 women (mean ±SD age: 24.5 ±1.4 yrs). The majority of the pregnancies were unplanned (87.5%; n=21). The majority of women (82.6%; n=19) were not observed throughout the pregnancy and were diagnosed during delivery (69.6%; n=16). Only 4 women (17.4%) received ARP prenatally and had a median VL of 33,860 (range:10,800-36,500) copies/mL at time of delivery. The majority of women (78.3%; n=18) had a history of IDU and hepatitis C (74%; n=19) co-infection. Caesarian section was performed in 26.1% (n=6). ARP during labor and postpartum was administered to 95.7% (n=22) of women/infant pairs. A total of 23 live infants were delivered with 62.5% (n=15) premature birth (median 35 weeks: 32-37 weeks). Two infants were breastfed (12 and 20 weeks) until positive status was established in their mothers. More than a third of women (39.1%; n=9) abandoned their newborns to the residential care.

**Conclusions:** The most significant barriers to successful PMTCT in our study were lack of prenatal care and late identification of HIV. Early identification and linkage to care of women at risk for MTCT, retention of women with IDU in care through the drug replacement and addiction therapy programs for the pregnant women are needed to increase the rates of successful PMTCT in Russia.

*No conflict of interest*

**Abstract: AB_37**

*Prevention of Mother-to-Child transmission*

**Progress in Reducing Infant HIV infection among HIV exposed Infants: Trends seen at the Mulago National Referral Hospital, Kampala Uganda; 2001-2011**

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*No conflict of interest*
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Background: Mother to child transmission of HIV (MTCT) remains high in Sub-Saharan Africa, despite increasing efforts to reduce it over the last decade. Antiretrovirals (ARVs) used during the perinatal period significantly reduce MTCT, as has been shown in developed countries. ARVs for prevention of MTCT became available in Uganda in early 2000. However, universal access to PMTCT services was not available until 2003, when single dose nevirapine (sdNVP) was recommended countrywide as standard of care.

Objective: To assess trends in early infant HIV infection at Mulago Hospital from 2001 to 2011.

Methods: Mulago National referral hospital offers rapid same day HIV testing during antenatal and at labor/delivery. Since 2001, Mulago hospital has provided ARVs for prevention of mother to child Transmission of HIV (PMTCT). From 2001-2005, sdNVP was the only PMTCT option available. In 2006, combination maternal ARVs (zidovudine (ZDV) or ZDV/3TC plus sdNVP with a ZDV/3TC 'tail', along with ART for women with CD4 <350, were introduced. Newborns initially received peripartum sdNVP and since 2010 extended NVP during breastfeeding. Infant DNA PCR testing was offered from 6-weeks of age.

Results: Over 8,000 HIV exposed infants have been tested at Mulago since 2001, with increasing numbers tested in the latter years. The percentage of infants who were HIV infected at age 6-12 weeks reduced from 16.1% in 2001 to 2.5% in 2011. Use of complex antenatal ARV regimens has increased steadily from 12.3%(395/3219) in 2006 to 71.7% (2162/3017) in 2010.

Conclusion: There has been major progress in reducing early infant HIV infections at the busy Uganda National hospital using combination ARVs; and with ART for sicker women. Further efforts to improve ARV adherence and reduce loss to follow up are underway with the goal of zero MTCT.

No conflict of interest

Abstract: AB_38

Prevention of Mother-to-Child transmission

Evaluation of an HIV educational intervention in an antenatal clinic in Odessa, Ukraine

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Background: Primary prevention of HIV infection in women of childbearing age is one of four ‘prongs’ in the global strategy for the prevention of HIV infection in infants. A prerequisite for HIV prevention is accurate knowledge among the general population of how HIV is transmitted and of strategies for preventing transmission. For pregnant women, knowledge of mother-to-child transmission (MTCT) and its prevention may also be important for uptake of antenatal services. Antenatal HIV prevalence in Ukraine is the highest in Europe at 0.55% (0.9% in Odessa). WHO, CDC and UNICEF have jointly developed educational tools to support pre-test counselling of pregnant women, consisting of a desktop flipchart to facilitate group counselling and booklets for women to take away. We investigated whether implementation of these tools in Ukraine led to improved HIV knowledge.

Material and methods: Two cross-sectional surveys of HIV knowledge were conducted among pregnant women attending an antenatal clinic in Odessa before and after clinic-wide introduction of the tools (phase 1 (P1), 2010, and phase 2 (P2), 2011). The questionnaire was anonymous, self-completed and included 27 questions, taking 10-20 minutes to complete.
The chi-squared test was used for categorical comparisons, and negative binomial regression models used to compare total HIV knowledge scores across the two phases.

**Results:** In total, 467 women took part (238 in P1 and 229 in P2; median age 27 vs. 26 years respectively, \(p=0.02\)). There was no difference by phase in timing of antenatal care initiation (median 12 weeks gestation), proportion who were parous (37%, 174/467) or educated until \(\geq 19\) years (76%, 308/401) \((p>0.1\) for all). There was a significant improvement in general HIV knowledge, with total HIV knowledge scores (sum of 27 responses) 13% higher in P2 than P1 (95%CI 7-19%, \(p<0.01\), adjusting for age and education). Adjusting for study phase and age, women leaving education at \(\leq 18\) years had total HIV knowledge scores 13% lower than those educated until \(\geq 19\) years (95% 8-19%, \(p<0.01\)).

In P1, 77% (n=184) correctly identified condom use as a way to prevent sexual HIV transmission, increasing to 88% \((n=201)\) in P2 \((X^2=8.82\) \(p<0.01\)). In P1, 51% \((n=122)\) of women knew that not all infants born to HIV-positive women will themselves be infected, increasing to 64% \((n=147)\) in P2 \((p<0.05)\). The proportion identifying three routes of mother-to-child transmission (MTCT) increased but remained low (9% \((22/238)\) in P1 and 17% \((40/229)\) in P2, \(X^2 =6.85\) \(p<0.01\)), with no increase in the proportion identifying three methods of preventing MTCT (i.e. antiretroviral drugs for mother, antiretroviral drugs for infant, avoidance of breastfeeding) (8% \((38/467)\) overall, \(X^2=0.02\) \(p=0.90\)).

**Conclusions:** Educational tool implementation was associated with modest increases in HIV knowledge from low starting levels in this pregnant population, but specific knowledge of MTCT remained low. Although understanding of MTCT risk/routes significantly increased, knowledge of interventions to prevent MTCT did not improve. Poor HIV knowledge among this sample of young, sexually active women, mostly with a high level of education, demonstrates the need for more effective HIV awareness and prevention strategies in Ukraine.

*No conflict of interest*
inconsistencies and missing values. Chi square test for trend was carried out for evidence of statistical significance in uptake over time for HIV counseling and testing, seroprevalence and uptake of prophylaxis for both mothers and infants.

**Results:** The program is one of the largest in the country, supporting 434 sites out of 2,025 nationally. From 2000 through 2010, 519,679 women received HIV counseling and testing; 6.9% tested positive. Over 96% of women counseled accepted testing and 99% of those tested received results. There was a statistically significant increase in the proportion of women tested and the proportion of women tested who received their results ($P<0.001$, Chi Square test for trend). Maternal seroprevalence decreased from 10.3% in 2000 to 5.3% in 2010 ($P<0.0001$; Chi Square test for trend). Maternal antiretroviral (ARV) prophylaxis uptake increased from 37.1% in 2000 to an average of 84% over the 11-year period. ARV prophylaxis uptake among HIV-exposed infants increased from 37.7% in 2000 to 48% in 2010.

**Conclusion:** The program’s integrated public-private partnership increased access to services. Quarterly supervision, mentoring and feedback from program data collected motivated service providers to improve the quality of care as suggested by the statistically significant increase in testing and receiving results. Infant ARV uptake is lower and remains a major challenge due to loss to follow-up, restrictive governmental dispensation policies, frequent change of national drug protocols, and drug stock-outs. CBCHS is working to improve supply chain management, infant follow-up (including early infant diagnosis) and linkages to care and treatment. Non-governmental organizations and governmental providers can collaborate to scale-up high quality PMTCT services that are sustainable and effectively monitored, evaluated and supervised.

*No conflict of interest*

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**Abstract: AB_40**

Prevention of Mother-to-Child transmission

**Use of peers and community laypersons improves postnatal clinic follow-up and Early Infant HIV Diagnosis in urban and rural health centers in Uganda**


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**Background:** Effective Prevention of Mother to child Transmission of HIV (PMTCT) relies greatly on follow-up of HIV infected women and infants from antenatal, through postnatal, to end of breastfeeding period. In Uganda, postnatal follow-up remains below 50% creating a missed opportunity for linkage to comprehensive care and EID. We evaluated the use of HIV peers and community lay persons to improve PNC follow up and EID.

**Method:** HIV infected women recruited from antenatal clinics at three urban clinics (Mulago-358, Rubaga-80 and Mengo-80 hospitals) and one rural health centre (Mpigi Health centre IV-40) between April 2009 and July 2010. The women were followed from enrolment during antenatal care through delivery; thereafter infants were followed postnatally at 6 weeks, 10 weeks, 6 month and 9 months. Peers, community lay persons and Village Health teams (VHTs) were identified and trained in basic PMTCT and reproductive health (RH). They were assigned to study clinics to supported
study participants, their partners and infants through provision of health education, counseling, home visits, and phone call reminders. PNC follow-up was measured as a proportion of mother-infant pairs that returned for postnatal follow up over expected.

**Results:** A total of 558 participants were recruited for the study, 40 mother-baby pairs were censured before 6 weeks PNC (11 Stillbirths, 22 infant deaths before 6 weeks of age, 4 maternal deaths, 3 participant withdrawal). At the postnatal six-week visit, 74% (385/518) of the infants returned and 99% of those who returned (381/385) were tested for HIV infection. Only 3.4% (13/385) of the infants tested had a positive HIV DNA PCR. Follow up at 6 week PNC follow-up visit was 90% (70/77) at Mengo, 88% (65/74) at Rubaga, 69.1% (228/330) at Mulago and 59.5% (22/37) at Mpigi. However, follow-up reduced overtime at 10 weeks, 6 months, and 9 months to 58%(303/518), 37%(192/518), 46% (238/518) and 33%(171/518) of the infants returned respectively.

**Conclusions:** Use of Peers and lay community persons led to an increase in postnatal follow up of HIV infected women, from below 50% to over 70% and EID of infants at the six week visit. However, follow-up of the infants through 9 months of age still requires strengthening.

*No conflict of interest*

**Abstract: AB_41**

*Implementation research on PMTCT and pediatric treatment programs*

**The need for Long-term Surveillance of Antiretroviral-exposed Infants**

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**Introduction:** Antiretroviral therapy has had a significant effect on improving maternal health and reducing mortality, as well as preventing the transmission of HIV to infants. As maternal triple-drug use increases, it is critical to enhance surveillance for complications in pregnancy and [the] long-term outcomes in infants.

The Antiretroviral Pregnancy Register is an ongoing international registry started in 1989 to collect reports from healthcare providers about adverse outcomes, such as birth defects or other abnormalities among infants born to women taking antiretrovirals during pregnancy.

**Materials and Methods:** In an analysis of the Antiretroviral Pregnancy Register, the researcher and colleagues analysed 700 of 3200 reported births from January 2001 to January 2011. The researchers compared the prevalence of pre-term births at less than 37 weeks into the pregnancy, at less than 32 weeks, birth weight under 2500g, and birth weight under 1500g among infants exposed to one antiretroviral, two or more antiretrovirals (combination therapy) that included a protease inhibitor (PI), and combination therapy that did not include a PI.

**Results:** No differences were reported in pre-term births and birth weight under 2500g in those newborns exposed either to one drug or to a combination of antiretrovirals. However, more infants exposed to combination therapy that included a PI were born weighing less than 1500g (17.4%) than those exposed to combination therapy without a PI (14%). Pre-term birth (under 37 weeks) was higher in those women on a PI-containing regimen than without, 14.1% compared to 11.8% (p 0.003). However, there was no significant difference in the proportion of pre-term births that occurred before 32 weeks of gestation according to the dose of drug the mother took.

**Conclusions:** The prevalence of birth weight under 1500g in those exposed to a combination that included a PI, while higher than in those exposed to a combination without a PI, was the same as those exposed to one antiretroviral and was protective against pre-term birth under 32 weeks (p 0.05). Nonetheless, the prevalence of birth weight under 1500g was lower in all combination groups than in previously published reports of cohorts of HIV-exposed newborns with no antiretroviral exposure. Very low birth weights, the researcher cautioned, are seen in very small numbers of infants. For example, in their analysis of 10,000 live births, 188 babies were born weighing less than 1500g.

*No conflict of interest*
Implementation research on PMTCT and pediatric treatment programs

Pre-Term Delivery in Mothers Receiving HIV Treatment in Nkwen Village: More Research Needed Before Changing Guidelines

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Introduction: Antiretroviral therapy in HIV-infected women during peri-partum for their own health and for the prevention of HIV transmission to their infants is recognised as a highly effective public health strategy. However, the link between a PI-based regimen and the risks of preterm delivery (before 37 weeks of pregnancy) continues to be controversial.

Materials and Methods: Randomised Clinical trial carried out amongst 530 HIV Sero-positive mothers on ARVs. The author looked at risk factors for preterm delivery in a cohort of HIV-infected pregnant women with CD4 cell counts under 200 cells/mm³ randomised to get either PI-based regimen (lopinavir/ritonavir/zidovudine/lamivudine) or NRTI-based regimen (abacavir/zidovudine/lamivudine) at 26-34 weeks of pregnancy in a clinical trial to prevent mother-to-child transmission. He also looked at maternal weight gain in late pregnancy and infant disease and death rates up to six months of age. Poor weight gain is known to be a risk factor for preterm delivery. PI-based regimens are known to cause gastrointestinal problems and adverse metabolic effects. Maternal change in body mass index (BMI) one month after the start of ART was compared according to treatment arm and delivery (preterm compared to term).

Results: Among women (267) in the PI arm preterm delivery rates were higher than among the 263 women in the NRTI arm, 21.4% compared to 11.8%, p=0.003. The PI-based regimen was the most significant risk factor, (OR: 2.03, 95% CI: 1.26-3.27, p=0.004). While median change in body weight in those in the PI arm was lower than in the NRTI arm one month after starting ART, there was no significant association with preterm delivery. Serious infant illness, defined as hospitalisation and death up to six months of age, did not differ by maternal regimen. This is probably because most preterm deliveries would have been near term. The highest rate of preterm delivery was seen in those who started ART later regardless of treatment arm, while HIV-infected pregnant women on a protease-inhibitor (PI) triple antiretroviral regimen were twice as likely to have a preterm delivery compared to those on a triple nucleoside reverse transcriptase inhibitor (NRTI) regimen. Approximately 1/3 of those who delivered preterm had had ART for less than thirty days. The highest rate of preterm delivery was seen in those who started ART later regardless of treatment arm.

Conclusions: The researcher also highlights the unexplained finding of the considerable lower rate of preterm delivery in the NRTI arm. He suggests that data from the same setting comprising women with similar baseline CD4 cell counts but who had been on a simplified prophylactic regimen, for example, zidovudine and/or single-dose nevirapine, would be helpful for comparison. PI-based ART regimens are a critical component of PMTCT and treatment programmes with proven benefits for maternal and child health. Conclusively, the researcher cautions that further research is needed before making recommendations about ART during pregnancy and for PMTCT as a consequence of the risk of pre-term delivery attached to any regimen.

No conflict of interest

Abstract: AB_43

Implementation research on PMTCT and pediatric treatment programs

Exploring Facilitators and Barriers to Participation of HIV-Exposed and HIV-Infected Children in Care and Treatment Services in Mozambique

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Introduction: Despite improvements in HIV pediatric care and treatment programs in Mozambique, engagement and retention of HIV-exposed and infected children in these services remain challenging. Understanding the reasons behind these challenges requires further inquiry. The Elizabeth Glaser Pediatric AIDS Foundation conducted a qualitative study in August 2011 – January 2012 to identify barriers and facilitators to HIV testing, enrolment into care, and follow-up services for children in Mozambique.

Material & Methods: Four participant groups—parents/caregivers with an HIV-exposed or infected child 0-14 years old, grandmothers, healthcare professionals providing pediatric HIV services, and community leaders—were recruited from seven health facilities and surrounding communities in Maputo City, Maputo Province, and Cabo Delgado Province (CDP) to participate in this study. In total, there were 298 participants (219 focus group participants and 79 interview respondents). Transcripts were transcribed and translated into Portuguese (for interviews and discussions conducted in local languages). Qualitative data were coded independently by two study staff members using MAXQDA; discrepancies were discussed and resolved. Data were organized by the most frequently mentioned barrier and facilitator codes for each participant group and by level (individual/caregiver, interpersonal, facility, and community). Recurrent themes and patterns were identified and comparisons made by region.

Results: The most frequently reported individual-level barriers to engaging children in HIV services were alternative care-seeking due to perceptions of traditional or spiritual causes of disease, disbelief in positive test results, fear of death, and a general lack of willingness to attend facilities. While present in all regions, the alternative care barrier exerted its strongest influence in CDP. The lack of willingness was more prevalent in Maputo Province and City. The most significant interpersonal-level barrier was fear of disclosure—this was the most reported barrier overall in Maputo Province and City, but was rarely mentioned in CDP. Poor service at facilities, such as long waiting times and difficulties obtaining drugs at the pharmacy, was cited in all groups. Traditional beliefs and customs and lack of social support were the most frequently recurring community-level barriers reported, although the latter was most often mentioned by healthcare professionals. Overall, there were fewer facilitators to care mentioned across groups. Facilitators were largely at individual and facility levels. All groups most often reported that children displaying visible illness and having hope for children's future motivate caregivers to go to facilities. The most commonly cited facility-level facilitators were perceptions that the facility was the appropriate place for HIV care and treatment, healthcare professional relationships, and institutional factors, such as free services and medications and service integration. The most significant interpersonal- and community-level facilitators were household decision-maker support for HIV care and treatment for children and social support, respectively.

Conclusions: Interventions to improve engagement and retention of HIV-exposed and infected children need to capitalize on feelings of hope for children's future and the understanding that HIV care and treatment is available at health facilities and critical to child health and survival. Strengthening community linkages and messaging to promote these beliefs and improving facility services (e.g., patient flow, pharmacy management) could counteract many documented barriers.

No conflict of interest

Abstract: AB_44

Implementation research on PMTCT and pediatric treatment programs

Treatment outcomes among children on antiretroviral therapy in Beira: an experience from decentralised HIV/AIDS service provision
Background From March 2010, the Ministry of Health began to decentralise antiretroviral therapy (ART) services from Beira Central Hospital (BCH), which began ART services in 2004, to health centres (HCs). About 627 children enrolled on ART at BCH were transferred to six HCs. With funding from UNICEF, Doctors with Africa CUAMM, which had been supporting ART service provision at BCH, began to support the provision of decentralised ART at four of the health centres. This study aimed at finding out whether treatment outcomes among children transferred from BCH to the HCs differed from those of children enrolled directly at the HCs.

Methods This was a retrospective cohort study of children on ART at four HCs which cater for about 87% of children on ART in Beira. Data were extracted from patients' files from March to July 2011. The exposure of interest was place of ART enrolment and the outcomes were loss to follow-up, mortality and overall attrition. Kaplan Meier plots were used to visually compare the cumulative probability of outcomes by place of enrollment. Crude and adjusted hazard ratios (HR) were estimated using Cox regression. The study was approved by the district health authorities.

Results Nine hundred and four children (47.5% female) with an analysis time at risk of 1,847 person years were studied. Of these, 434 (48.0%) were enrolled at the HCs and the rest were transferred from BCH/other health facilities. There were 47 deaths, and 63 children were lost to follow-up. After adjusting for confounders, children transferred to HCs had reduced mortality (HR 0.19, 95% CI: 0.06-0.63) and reduced overall attrition (HR 0.45, 95% CI: 0.26-0.78) compared to children originally enrolled at the HCs. The difference in loss to follow-up between the two groups was however not significant (HR 0.56, 95% CI: 0.29-1.06, p=0.077).

Conclusion Children transferred to the HCs had lower mortality and attrition rates than those originally enrolled at HCs. There was no significant difference between the two groups of children in terms of loss to follow-up. Decentralisation of ART appears not to have negatively affected treatment outcomes among children transferred to the HCs compared to those enrolled directly at the HCs in Beira.

No conflict of interest

Abstract: AB_45

Implementation research on PMTCT and pediatric treatment programs

Scaling-up access to HIV treatment: comparing outcomes among children receiving treatment at mobile and hospital-based HIV clinics in rural Zambia

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Background: Travel time and distance are barriers to care for HIV-infected children in resource-poor settings. Decentralization is one of the strategies to scaling-up access to antiretroviral treatment (ART), but few such programs have been evaluated. We compared outcomes for children receiving care in mobile and hospital-based HIV clinics in rural Zambia.

Methods: Outcomes were measured within an ongoing cohort study of HIV-infected children seeking care at Macha Hospital, Zambia since September 2007. Children in the outreach group received ART from the Macha HIV clinic and transferred to one of three mobile outreach clinics administered by Macha Hospital. Children in the hospital group received ART at the Macha...
HIV clinic, and reported Macha Hospital as their nearest healthcare facility.

**Results:** 46 children in the outreach group and 41 children in the hospital group were included. The median time between enrolment and transfer to the outreach clinic was 10.2 months (IQR: 5.7, 14.9). After transfer to the outreach clinic, travel time was significantly shorter and fewer caretakers used public transportation (before: 47.8%; after: 2.8%; p<0.0001). Consequently, 44.4% of caretakers reported lower transportation costs and 69.4% had fewer obstacles with transportation. Caretakers reported receiving the same quality of care, although some within the outreach group perceived the waiting time to be better but counseling services and physical examinations to be worse. At ART initiation, median age, weight-for-age z-scores (WAZ) and CD4% were similar for children in the hospital and outreach groups. Children in both groups experienced similar increases in WAZ and CD4%. Five children, all in the outreach group (12.8% vs. 0.0%; p=0.07), experienced virologic failure after their transfer. The median percentage of visits with full adherence (>95%) was significantly lower in the outreach compared to the hospital group (65% vs. 84%; p=0.02).

**Conclusions:** Despite similar clinical and immunologic outcomes, children in the outreach group were less likely to achieve virologic suppression, potentially due to lower adherence. Continued adherence counseling is critical for the success of decentralized care.

*No conflict of interest*

**Abstract: AB_46**

Implementation research on PMTCT and pediatric treatment programs

PMTCT decentralization does not assure optimal service delivery: revelations from individual-level tracking of HIV-infected mothers and their infants

**Introduction:** As essential services for PMTCT are increasingly decentralized to antenatal care (ANC) sites, the consequences of shifting services from dedicated HIV care and treatment (C&T) clinics remain incompletely explored. We compared service delivery at ANC and C&T clinics in Kinshasa, DRC, a low HIV prevalence, resource-deprived setting.

**Material & Methods:** In 10/2010, an enhanced standard of care was introduced at 44 ANC sites: personnel were retrained to implement the 2010 WHO PMTCT guidelines including Option A and co-located post-delivery care, and were provided with new individual-level tracking tools and supportive supervision. Women were encouraged to enroll at either of two affiliated C&T sites for continued PMTCT and HIV care but could opt to receive AZT-based prophylaxis at ANC sites when it became available alongside CD4 testing in 2011. Antiretroviral therapy was available only at C&T sites.

**Results:** Of 1,233 HIV-infected women tracked between 10/2010 and 12/2011, 926 (75.1%) were newly diagnosed; 306/926 (33.0%) enrolled in C&T. Newly diagnosed women were more likely to receive CD4 testing (RR=2.2; 95% CI 1.9-2.6) and a WHO-recommended regimen (RR=1.6; 95% CI 1.4-1.8) if they enrolled in C&T than if they remained at an ANC site. Infants were more likely to receive a package of extended NVP, cotrimoxazole and DNA PCR testing at C&T than at an ANC site (RR=1.9; 95% CI 1.6-2.3). At ANC sites, 116 women received AZT-based prophylaxis and 91 received CD4 testing; 95 infants received the postnatal package.

**Conclusions:** Individual-level tracking of mothers and infants was feasible in Kinshasa and revealed that PMTCT services were delivered less effectively at sites historically focused on ANC rather than HIV C&T. While decentralization increased care access, its potential to further reduce vertical transmission cannot be fully realized without sustained training and supervisory support to ensure
optimal quality of service delivery throughout the entire PMTCT cascade.

No conflict of interest

Abstract: AB_47
Implementation research on PMTCT and pediatric treatment programs

HIV+ clinic volunteers improve uptake of comprehensive services by HIV+ pregnant women in Kinshasa, Democratic Republic of Congo: a randomized study

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Introduction: When PMTCT and HIV care and treatment (C&T) services are provided in distinct facilities, HIV+ pregnant women are often not linked to post-delivery C&T. Between 1/2008 and 8/2010, 2,017 women were identified as HIV+ at 44 maternities in Kinshasa, DRC, yet just 791 of these women presented to affiliated C&T centers for free, comprehensive services. Many obstacles to C&T uptake have been recognized, including a weak referral and tracking system, transportation difficulties, and denial of one’s diagnosis, and in various sub-Saharan African settings HIV+ clinic volunteers have provided peer support to mitigate such barriers. We assessed the effect of HIV+ clinic volunteers (‘mother mentors’) on uptake of C&T at affiliated centers by HIV+ pregnant women.

Material & Methods: In 10/2010, 16/32 Kinshasa maternities were randomized to receive an HIV+ clinic volunteer trained in basic motivational educational techniques, who encouraged (and accompanied) women to enroll in C&T. All sites also received an enhanced standard of care: personnel were provided with new tracking tools, intensified supportive supervision, and patient transportation reimbursement, and were retrained to implement the 2010 WHO PMTCT guidelines including Option A.

Results: Of 725 HIV+ women newly diagnosed between 10/2010 and 12/2011, 674 (93.0%) were offered and 513/674 (76.1%) accepted referral. Referral acceptance was no higher (cluster-adjusted RR=0.96; 95% CI, 0.80-1.15) at maternities with HIV+ volunteers (248/328, 75.6%) than without (265/346, 81.3%). Of 513 women accepting referral, 378 (73.7%) were referred to an affiliated care center. Among these women, uptake of C&T was greater (cluster-adjusted HR=1.39, 95% CI, 1.01-1.91) if the referring maternity had an HIV+ volunteer (126/197, 64.0% versus 96/181, 53.0%). The median time between referral and arrival was three days (IQR, 1-26).

Conclusions: In settings without co-located PMTCT and C&T services, HIV+ clinic volunteers are a promising approach to improve care uptake by HIV+ pregnant women.

No conflict of interest

Abstract: AB_48
Implementation research on PMTCT and pediatric treatment programs

Should PMTCT programs take into account socioeconomic indicators related to antenatal care seeking behavior?

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Background: The WHO recommends ≥4 antenatal care (ANC) visits during pregnancy, starting in the first trimester. Inadequate ANC can lead to increased morbidity and mortality for both mother and child. The antenatal period is particularly critical for HIV-infected women, as
this is when lifesaving prevention of mother-to-child transmission (PMTCT) regimens can be delivered. We determined if socioeconomic status (SES) is predictive of adequate ANC to inform scale-up of PMTCT services throughout DRC.

**Methods:** We conducted a household-based survey in Kinshasa, DRC. Stratified two-stage cluster sampling was used to select women ≥18 years old with a pregnancy in the last three years. Participants were interviewed about ANC experiences, as well as their demographic and household characteristics. We created a composite measure of SES using principal component analysis. Multivariate models accounting for sampling probabilities were used to assess associations between SES (low, medium, or high) and adequate ANC, defined by frequency and initiation.

**Results:** We interviewed 1,214 women who had a median age of 27 years. Fewer than 30% reported employment and 93% reported their highest level of education was at most secondary school. Among the 98% who sought ANC, 78% initiated care after the first trimester and 22% sought care <4 times. The odds of initiating ANC in the first trimester among women with low SES (odds ratio [95% confidence interval]: 0.45 [0.29, 0.68]) or medium SES (odds ratio [95% confidence interval]: 0.44 [0.29, 0.67]) was about half that of women with high SES. Women with lower SES also had lower odds of seeking ANC ≥4 times, with an odds ratio (95% confidence interval) of 0.29 (0.17, 0.49) for women with low SES and 0.70 (0.40, 1.21) for women with medium SES, compared to women with high SES.

**Conclusions:** Our results show that women with lower SES are less likely to receive adequate ANC. Low SES may pose significant barriers to seeking care due to associated costs, such as those for transportation, medications, and clinic fees. Program implementers cannot ignore SES-related barriers when designing and scaling-up PMTCT interventions.

**No conflict of interest**

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**Abstract: AB_49**

**Implementation research on PMTCT and pediatric treatment programs**

**Early infant diagnosis and access to pediatric HIV care: barriers and challenges in Abidjan, Ivory Coast in 2011**

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**Background:** WHO recommended a universal antiretroviral therapy for all HIV-infected children before 2 years of life in 2010 but this roll-out is a real challenge for national programs on identifying early these children. The national program in Côte d’Ivoire decided to scale up the early infant diagnosis (EID) using Dried Blood Spot (DBS). We described the access to pediatric HIV EID and care in Abidjan Côte d’Ivoire, in 2011, after the Ivorian post-electoral crisis and before the implementation of an international randomized clinical trial to assess simplified strategies for triple antiretroviral therapy in HIV-infected children initiated on treatment before two years of age in Africa.

**Methods:** A survey of the national indicators was provided about the coverage of Prevention of Mother-to-Child (PMTCT) interventions in 2010. A 6-month survey was undertaken from July to December 2011 in 27 health facilities delivering pediatric HIV services in Abidjan to monitor the process of EID of all HIV-exposed children < 18 months of age until the delivery of their results. Data from PCR register were extracted each month: number of DBS requested from the services, number of DBS performed and returned to centers, number of pediatric HIV infections identified and number of HIV-infected children oriented for HIV care.
Results: With a national HIV prevalence estimated to be 3.4% in 2010, Ivory Coast remains one of most affected countries in West Africa. In this country among the 900 centers providing prenatal health care, only 371 (41%) provided PMTCT interventions in 2010. In 2010, among the 16226 HIV-infected pregnant women identified, only 49% received antiretroviral drugs for PMTCT and only 24% of their offspring had access to EID. We noticed also regional heterogeneity in covering PMTCT services. From July to September 2011, in the Abidjan’s survey in the amount of the MONOD project, among the 756 HIV exposed children who had access to DBS EID, only 47% received their DBS results, varying from 66% to 24% according to month. Among the 34 HIV-infected children identified, only 50% were oriented to HIV pediatric care. Several barriers were identified in this context: the post-electoral period, the transition of strategic screening activities (transport and technical support) to local partners after the end of the Pediatric Elisabeth Glazer Foundation ones, the lack of transportation system of DBS samples, the excessive delay in returning back DBS results to health facilities, the lack of community and health care professional motivation to trace HIV-exposed children, stigma...

Conclusion: Too many missed opportunities for both the PMTCT and the access to early HIV infant diagnosis and care remain in 2011. Challenges still remain to improve early identification of HIV-infected children, reduce the DBS turnover round time and promote early orientation of HIV-infected children to appropriate HIV care. With the commitment of the National Program, it is crucial to identify sustainable mechanisms to promote a universal and early access to pediatric HIV care services in Côte d’Ivoire.

No conflict of interest

Abstract: AB_50

Implementation research on PMTCT and pediatric treatment programs

Factors related to loss to follow up among HIV infected children seeking clinical care: Experiences from a private health care facility from India.

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Introduction: Anti-retro viral treatment (ART) improves clinical and immunological outcomes among HIV infected children. Greater benefits are realized with better linkage and retention in care. Currently, there are ≥80000 HIV infected children in India. With rapid progression of HIV disease in young children, providing timely and continued care is crucial. Data from other resource poor settings show that HIV infected children present to care late in their disease with high mortality and lost to follow up rates. Country specific difference of HIV prevalence, co-existing infections and access to care facilities pose unique challenges for pediatric HIV programs in Indian context. We seek to understand profile of HIV infected children presenting to care and rates and determinants of lost to follow up (LTFU).

Material & Methods: This is a retrospective cohort study of all patients attending a pediatric HIV care program at Prayas, Pune. Medical and laboratory data was entered in access database by medical chart abstraction. ART naive HIV infected children presenting anytime during Aug 1998 to Dec 2011 and staying with family at the time of presentation were included in the study. Any study subject that did not visit the clinic for at least 6 months since their last visit was classified as LTFU. Kaplan Meir probabilities of LTFU and Log rank test was used for comparison between the subgroups. Cox proportional hazard model was fitted for the data to estimate risk of LTFU for different socio-demographic and clinical parameters at the time.
of entry to clinic. Statistical analysis was done using SAS 9.2 (SAS institute, Cary, NC, USA).

Results: Out of 333 children (0 to 18 years), 141 (42.34%) were girls, 156 (46.8%) had lost at least one parent. Majority (96.8%) were perinatally infected. The median age at entry to clinic was 7 years (IQR-6); 16% were below 3 years. 46% were in WHO clinical stage 3 or 4 and 42.6% had advanced or severe immune deficiency. Median age at ART initiation was 8 years (IQR-7.5).

Total 166 (49.8%) children were lost to follow up. Median time for lost to follow up was 38.4 months. LTF rate was highest during first 3 months of follow up. Probabilities for retention in care over the time varied according to age, parent’s vital status, clinical/immunological stage at entry to clinic; with significant difference across different age groups (p=0.007). Children who had lost both parents (HR=1.74, 95% CI 1.09 – 2.7) and of age <2 years at entry to the clinic (HR=1.94, 95% CI 1.04 – 3.6) were more likely to be lost to follow up.

Conclusions: Late presentation and high proportion of lost to follow up to care are major challenges for pediatric HIV care programs in India. Retention in the first year is a critical indicator of prolonged engagement. Provision of comprehensive family based care to prevent morbidity and mortality among parents is crucial.

No conflict of interest

Abstract: AB_51

Implementation research on PMTCT and pediatric treatment programs

Early infant HIV diagnosis results turnaround time and concordance between records from facilities and laboratories in Zambia

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Introduction: Initiation of infant ART continues to be low in developing countries due to delays in diagnostic testing and timely availability of results to care givers. In Zambia, 85,000 infants are estimated to be HIV exposed annually. Three laboratories and over 700 health facilities provide early infant diagnosis (EID) services. We assessed results reported for consistency and turnaround time (TAT) at laboratories and facilities.

Material & Methods: We conducted a retrospective records review of baby-mother pairs initially seen between April 2009 and March 2010 at 23 purposively selected health facilities to capture follow-up data for a 1-year period. PCR results extracted from facility records were traced back to the 3 originating EID laboratories to access concordance. The time between DBS collection and results receipts was also analyzed.

Results: Of 3,236 extracted facility records, 2,331 (72%) contained a PCR result, of which 1,376 (59%) could be linked to laboratory records. In 18 (1.3%) cases, laboratory and facility records results were discrepant. The result discrepancy rates associated with 2 laboratories was similar, 0.7% (8/1153) vs. 1.1% (1/90), but the rate in the third laboratory 6.8% (9/133) was significantly higher than that of the two other laboratories combined (p<0.0001). The median TAT was 37 days from DBS collection to result receipt at facility and 61 days to receipt by caregivers.

Conclusions: The median TATs of EID results were considerably long; probably due to delays in DBS transport to the laboratory and results return to facilities and patients. Innovative result transmission approaches like the SMS technology currently being piloted may help reduce TAT. Given these findings of discrepant results, and missing records, there is a need to strengthen documentation and monitoring systems to prevent and detect errors in results transmission that may lead to wrong diagnostic reports and care of HIV exposed infants.

No conflict of interest
Abstract: AB_52

Implementation research on PMTCT and pediatric treatment programs

Public Private Partnership for universal access to antiretroviral therapy in children: Costs of an evolving model for healthcare delivery in India

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Introduction: In India up to 80% of health expenditure is made out-of-pocket in the country's extensive private health sector. The state however runs an effective National AIDS control program, implemented largely through the public sector. For the national scale-up for pediatric HIV treatment, public-private partnerships could serve to increase access to antiretroviral therapy (ART). In this paper we discuss the costs incurred by the private healthcare providers and the public sector in the context of an existing PPP. The PPP model: The private institution contributes human resource, physical structure, equipment and maintenance facilities to the "ART center"; this is the primary responsibility of the private institution the partnership. The public health sector contributes antiretroviral drugs and medications for opportunistic infections. Both sectors contribute to routine laboratory investigations, such as CD4 counts. The Centre thus provides basic healthcare services at no cost to HIV-infected individuals. Paediatric HIV infections are managed at this centre with additional support provided by the paediatric infectious disease unit at the hospital.

Materials and methods: The costing study for pediatric HIV treatment was done at St. John’s Medical College Hospital, Bangalore India from a private healthcare provider perspective. The existing model for delivery for healthcare for children with HIV was studied. For costing, the sequential procedure was used. This involved identifying resources used in natural units (eg: time assessed in minutes), measuring resource use and pricing the resource. Sunk costs, (eg. costs of physical structures) were not included in this analysis. The costs were categorised into one time costs and recurrent costs. Recurrent costs were further categorised into fixed costs and variable costs. Fixed costs included costs of staff and overheads. Variable costs were the costs of medicines and laboratory investigations, i.e. CD4 count.

Results: Costs of care: The total number of children registered at the ART center was 187, of whom 100 were on ART. The total annual cost incurred by the PPP was 17,481.52 USD. Of the total annual cost, 39% (6851.00USD) was contributed by the private healthcare provider and 61% by the public sector. One-time costs incurred were 118.25 USD, fixed costs 2,667.98 USD and variable costs 13,053.23 USD. The total annual staff costs incurred were 4,142.27 USD, 95% of these costs were contributed to by the private organization. The total cost of care/child/year was 84.52 USD ie; 7.04 USD/month.

Conclusions: In our study most of the costs towards staffing were contributed to by the private institution while most of the costs towards medicines and investigations were contributed to by the public sector (60% of total costs). Public-private partnerships thus enable sharing of costs between private and public healthcare sectors, reducing public sector costs and enhancing access to healthcare through the dominant private sector. The model provides an opportunity to ensure universal access to antiretroviral therapy in children in the Indian context.

No conflict of interest

Abstract: AB_53

Implementation research on PMTCT and pediatric treatment programs

Evaluation of Early Infant HIV Diagnosis Laboratory Capacity in Zambia
Introduction: Zambian Early Infant HIV Diagnosis (EID) program started in 2006; there are currently 3 laboratories processing dried blood spot (DBS) for EID from over 700 health facilities. An evaluation of EID health facilities found a turnaround time (TAT) of 61 days from DBS collection to result receipt by caregivers, delaying commencement of ART for HIV-positive infants. We evaluated current infrastructure, testing quality and TAT, human and diagnostic capacity of these laboratories.

Material & Methods: Laboratory managers representing the EID laboratories were interviewed in April 2011 using a semi-structured questionnaire covering existing quality of testing, equipment maintenance, procurement and supply chain, training and retention of personnel, data management and record keeping, and TAT of PCR results.

Results: The three EID laboratories met PCR layout requirements. With 4-5 dedicated staff each, they processed a monthly average of 944, 1200, and 1500 DBS from 179, 377, and 108 health facilities respectively, and all participated in an external quality assessment program where two scored 100%, and one scored 90% in the previous year. Operating procedures were standard across the laboratories with minor variations; but laboratories lacked standard data management and equipment maintenance systems, formal quality assurance program and a national testing algorithm. One laboratory reported reagent stock-out in the prior 3 months. The average TATs within the laboratories from DBS sample reception to PCR results readiness was 4 days for two laboratories and 5 for the third.

Conclusions: Zambia has a well-functioning EID laboratory system with adequate infrastructure, staff and laboratory practices. DBS processing time within laboratories is short; suggesting that the long overall TAT is attributable to factors outside the laboratory. Zambia needs a national testing algorithm, standardized equipment maintenance and data collection systems, and internal quality assurance programs to improve the laboratories' effectiveness in providing timely and accurate infant HIV diagnosis.

No conflict of interest

Abstract: AB_54

Co-infections in HIV-infected children

Group B streptococcus (GBS): Institutional policies for prevention and rates of infection in HIV-infected women and their infants in Latin America

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Background: Intrapartum antibiotic prophylaxis (IAP) for pregnant women with rectovaginal group B streptococcal (GBS) colonization prevents early onset neonatal GBS disease. Rectovaginal GBS colonization may be more common among HIV-infected pregnant women, and HIV-exposed, uninfected (HEU) infants may be at higher risk of neonatal GBS disease than infants of HIV-uninfected mothers. Little is known about GBS prevention policies for HIV-infected pregnant women in Latin American countries. The objective of this study is to describe the neonatal GBS prevention policies at 12 Latin American clinical sites participating in the NICHD
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(Eunice Kennedy Shriver National Institute of Child Health and Human Development) International Site Development Initiative (NISDI) Longitudinal Study in Latin American Countries (LILAC) study and to determine the rates of GBS maternal colonization and maternal and neonatal disease among the enrolled HIV-infected women and their infants.

Methods: Standardized site surveys were used to assess institutional GBS prevention policies and practices. Data collected as part of the NISDI study were used to determine the maternal rectovaginal GBS colonization rate and rates of maternal and neonatal GBS disease.

Results: Nine (75%) sites had a GBS policy, including 7 that performed rectovaginal GBS screening on all women. All sites with a GBS policy used penicillin or ampicillin for IAP. Fifty seven percent of participants were screened for GBS. Rectovaginal GBS colonization rate at sites reporting routine screening was 8.3% (19/228, 95% confidence interval [CI]: 5.1 – 12.7%). GBS disease occurred in two women (2/401; 0.5%; 95% CI 0.06 – 1.8%) and no infants (0/398, 95% CI: 0.0 – 0.9%).

Conclusions: Improved efforts to implement GBS prevention policies and continued surveillance for GBS disease are needed to better understand the impact of GBS in HIV-infected pregnant women and their infants in Latin American Countries.

No conflict of interest

Abstract: AB_55

Co-infections in HIV-infected children

Prevalence of Opportunistic Infections (OIs)in HIV infected Children undergoing Antiretroviral Therapy at Baylor-Uganda, Mulago Hospital

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Introduction: Highly active antiretroviral therapy has been reported to reduce prevalence and severity of opportunistic infections (OIs) in HIV disease. However, there is a paucity of data in African children to support this. This paper presents point prevalence of opportunistic infections from a three year observational study at the Baylor-Uganda COE.

Materials and Methods: A total of 108 HIV infected children aged 3 months to 17 completed years were sequentially enrolled onto this prospective cohort and started on highly active antiretroviral therapy in 2006. All clinical assessment findings including the occurrence of OIs were recorded on standardized forms, viral load and CD4 assessments made at baseline, 1 month, subsequently every 3 months for the first year, and then 6 monthly until the end of the study. Data was entered into Epi Info version 3 and exported to SPSS 12.0 for analysis. Occurrence of OIs was summarized into proportions at months 6, 12 and 36 time points.

Results: Of the 108 participants enrolled 51% were female; the median age was 6 years IQR (1-10). Fifty three percent compared to 41% received EFV and NVP based regimens, while 4% and 2 % were on triple NRTIs and PI based regimens respectively. The overall adherence rate was 95% using a ≥ 95% level. Median CD4 % at baseline was 9% (IQR 4-15) and increased by 20, 22 and 20 at 6, 12 and 36 months respectively. At baseline OIs included upper respiratory tract infections (URTI-23%), skin and scalp infections (35%), ear infections (2%), pneumonia (9%), tuberculosis (11%), oral candidiasis (11%), and Kaposi’s sarcoma (3%). Subsequently prevalence of URTI, skin/ scalp and ear infections was 46%, 29% and 5% at 6months; 54%, 25%, 0% at 12 months; and 43%,1% and 0.01% at 36 months. Stage III and IV events seen at 6 months (n=99) included pneumonia and tuberculosis (4%), oral candidiasis (3%) and Kaposi sarcoma (2%). There were no severe infections at 12 and 36 months.
**Abstract: LB_15**

**Knowledge, attitude and prevention of HIV/AIDS among senior secondary students in Nigeria**

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**Background:** HIV/AIDS is an important public health burden globally and it is a significant cause of morbidity and mortality in the developing countries. It is the third largest worldwide disease, behind India and South Africa. Adolescents are at risk of HIV infections especially in the developing countries. Because few control programme target this age group, there is paucity of information on the knowledge of the disease among adolescents. This informed our carrying out this study.

**Aims & objectives:** To determine the knowledge of urban and rural Nigerian secondary school students on HIV/AIDS.

**Methods:** Information were obtained from 280 Nigerian senior secondary school students using a stratified randomized sampling technique. The site of study were located in 2 urban and 2 rural schools in Osun State. Structured questionnaires were administered to the Subjects. Information obtained included socio demographics, knowledge of HIV disease and its transmission. The results obtained were analyzed using SPSS version 17.

**Results:** There were 280 students consisting of 153 girls and 127 boys (female to male ratio of 1.2:1) in the study. The ages of the students range from 13 to 24 years. Most of the student, 240 (86%) had heard about HIV/AIDS previously. A fewer proportion of these, 195 (69.9%) knew that it was a germ while a comparable proportion, 196 (76%) knew the full meaning of HIV. Two hundred & eight (74.3%) of the students knew that sexual intercourse was a risk factor for HIV transmission. Eighty eight (31.3%) knew that HIV could be transmitted through blood transfusion, 95 (33.9%) stated that HIV could be transmitted by contaminated object such as clippers and sharp object. A hundred and thirteen (40.4%) practiced abstinence while 149 (53.2%) responded that use of condom to prevent HIV infection.

On the other hand, 136 (48.6%) and 176 (62.9%), responded respectively that HIV is curable and treatable. Forty eight students (17.1%) responded that HIV can be transmitted through hand shake with infected person while 43 (15.4%) eating with infected person, while 60 (21.4%) said it can be transmitted when sleeping on the same bed with an infected person. More of the students in the rural areas tend to have better knowledge of HIV risks, curability, and effect of condom use and this was statistically significant at P<0.01.

**Conclusion:** It is concluded that most of these students have heard about HIV/AIDS. However, their knowledge of the virus, its means of transmission and mode of preventing infection from this virus, is poor. Concerted efforts should therefore be made to communicate the right information to them.

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**Abstract: LB_16**

**The development of substance use behaviors in perinatally HIV-infected adolescents: A longitudinal study.**

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**Background:** Evidence suggests perinatally HIV-infected (PHIV+) youth initiate substance use during adolescence. Substance use in HIV-infected adults is associated with poor health outcomes, including complicated disease progression and poor antiretroviral treatment adherence. It may also increase the likelihood of sexual risk behaviors, placing others at risk for secondary HIV-transmission. The developmental course of substance use and disorders is unknown in PHIV+ youth and may have important treatment implications.

**Methods:** Data are from three waves of a US longitudinal study of mental health and risk behavior in an urban sample of PHIV+ and perinatally exposed but uninfected youth (PHIV-) (n=340; 60.6% PHIV+; 50.5% male; 9-22 years; 45.9% African American, 50.0% Hispanic). Substance use was assessed using the Diagnostic Interview Schedule for Children-IV youth version) and compared across ages and by HIV-status. Development of substance use was assessed by latent class growth mixture modeling. Logistical regression assessed relationships between trajectories, HIV-status, and demographics.

**Results:** By the third wave, 53.31% of adolescents had experimented with drinking and 27.69% with marijuana with no difference between PHIV+ and PHIV- youth. PHIV+ adolescents had greater prevalence of SUDs (n=25, 12.13%) than PHIV- youth (n=10, 7.46%) but the difference was not significant (p=0.165). There were two trajectories of frequency of alcohol and marijuana use: Non-Use/Experimenters (Alcoholn=279, 82.06%; Marijuana,n=294, 86.76%) and Early Users (Alcoholn=61, 17.94%; Marijuana,n=45, 13.24%). The Non-Use/Experimenters groups had a later onset of alcohol and marijuana use behaviors than the Early User groups. Belonging to the Early User group for alcohol increased the likelihood that the adolescent belonged to the Early User group for marijuana use and vice versa. There were no differences in risk groups by demographic characteristics or HIV-status.

**Conclusions:** Unlike behaviorally infected HIV+ youth, PHIV+ youth may not be at a heightened risk for developing and maintaining SUDs in adolescence. Nonetheless, there is a cohort of PHIV+ youth with problematic substance use including early experimentation and SUDs. Despite age-normative development of substance use, given the harmful implications of SUDs for HIV+ individuals, it is critical to consider the treatment ramifications for HIV+ youth.

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**Abstract: LB_17**

**Sexual Health Knowledge in a Sample of Perinatally HIV-infected and Perinatally-exposed Uninfected youth.**


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**Background:** Perinatally HIV-infected (PHIV+) youth, once expected to not outlive childhood, are reaching adolescence, an age of sexual exploration, in relatively large numbers. Yet, it is unclear whether they receive accurate and adequate information about sexual health. This is a matter of serious public health concern in New York City, where 1 out of 4 teens have a sexually-transmitted disease. This study describes STD/pregnancy knowledge among a sample of PHIV+ youth living in NYC.

**Methods and Materials:** Cross-sectional data were drawn from the baseline interviews of a longitudinal study examining mental health and behavioral risk outcomes in PHIV+ youth and perinatally exposed, but uninfected (PHIV-) youth (N=316; age range=9-16 years; 50% female; 40% Latino; 45% African-American; 60% PHIV+). Demographics were collected from the caregiver and youth. Child sexual health knowledge was assessed using a questionnaire comprised of 19 items on STD and pregnancy. Adolescents answered each item “True,” “False” or “Unsure.” For every correct answer, youth scored one point. Caregiver and youth each reported whether they discussed sex, STD and
pregnancy prevention and birth control; if either reported having discussed one of these topics they were asked to report the number of times the topic was discussed in the previous month. T-tests were used to compare mean scores on sexual health knowledge between various youth categories: gender, ethnicity, HIV status, PHIV+ disclosure and caregiver’s HIV status, whether or not youth was residing with a biological parent, and youth-caregiver sexual health communication. Correlations were calculated for scores on sexual health knowledge and age, caregiver education, household income, and frequency of youth-caregiver sexual health communication.

**Results:** Youth who reported talking about sex with their caregivers had significantly higher sexual health knowledge than those who did not (mean STD knowledge scores are 8.54 vs. 5.84 respectively, p<.001). Among PHIV+ youth, those who were disclosed (72%) scored significantly higher on sexual health knowledge than those unaware of their HIV status (mean scores 7.27 vs. 4.70, p<.001). Youth age and more frequent parent-youth conversations about sex and pregnancy were positively correlated with STD/pregnancy knowledge scores (r=0.489, p<.001 and r=0.290, p<.001, respectively). Participants in both groups answered only 35% of the questions correctly (mean=6.6 out of 19). When comparing PHIV+ and PHIV- youth, some significant differences emerged: 30% of PHIV- youth correctly identified that one could get an STD and HIV at the same time vs. 18% of PHIV+ youth (p=.028); 21% of PHIV- vs. 32% of PHIV+ youth correctly identified that a girl can get pregnant if the male pulls out before ejaculation (p=.039); 24% of PHIV- youth vs. 36% of PHIV+ youth correctly identified that using a douche after sex is an ineffective method of birth control (p=.026).

**Conclusion:** Both PHIV+ and PHIV- youth had significant deficits in STD/Pregnancy knowledge. The results indicate the need for sexual health education, particularly for PHIV+ youth who are more susceptible to contracting STDs and for whom STDs increase the risk for secondary transmission of HIV to their partners. Data also suggest that interventions focused on caregiver-child risk communication may be important for prevention.

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**Abstract: LB_18**

**Exploratory Analysis of Cognitive and Emotional Functioning in Perinatally HIV-Infected and Affected Youth, in a Bio-psychosocial Assessment Program**

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**Background:** Perinatally HIV-infected and HIV-affected youth experience more emotional difficulties during their child and adolescent development than the general population. In the pre-HAART medication era, children infected with HIV presented with neuropsychological deficits related to their HIV disease. These deficits have been reported less frequently during the post-HAART era. HIV-infected and affected youth are at greater risk for poor developmental outcomes than their uninfected peers; which include social skills, behavioral, educational and psychiatric difficulties. This study compares HIV-infected and affected youth’s cognitive and emotional functioning over a 3-year period, to assess their needs, and to improve overall functioning and medical outcomes.

**Methods:** 118 HIV-infected and affected youth (53% male; 75% perinatally infected), ages 6 – 29 years (mean = 18.65 years), receiving care in an urban New York City Hospital Clinic, participated in the Biopsychosocial Assessment Program (BAP) from 2006 – 2011. The BAP is an empirically guided comprehensive screening program, designed to annually assess mental health, cognitive, and academic needs. Participants completed a cognitive screen (Wechsler Abbreviated Scale of Intelligence - II); an achievement screen (Wide-Range Achievement Test -3rd Edition); clinical interview, and self-reported inventories assessing depression (Beck Depression Inventory or Children’s Depression Inventory) and anxiety (Beck Anxiety Inventory or Multidimensional Anxiety Scale for Children). Estimated Full Scale IQ (eFSIQ) and standard scores in math, reading
and spelling were obtained. An independent t-test was used to compare HIV infected and affected youths’ mean scores, per year, on the depression, anxiety, cognitive and achievement measures.

**Results:** When comparing HIV-infected (n=88; 75%) and affected youths’(n=29; 25%) cognitive scores in BAP years 1 and 2, HIV-infected youths’ estimated full scale IQ (eFSIQ) means were significantly lower than HIV-affected youth means (Years 1 and 2: HIV-infected eFSIQ - Low Average Range, HIV-affected eFSIQ - Average Range, \( p<.05 \)). In BAP year 3, no significant cognitive differences emerged. On the achievement measure for all BAP years 1-3, HIV-infected youths’ mathematics means were significantly lower than HIV-affected youths’ means (Year 1: HIV-infected mathematics means - Low Average Range, HIV-affected mathematics - Average Range, \( p<.05 \); Years 2 and 3: HIV-infected mathematics - Borderline Range; HIV-affected mathematics - Average range, \( p<.05 \)). Across all three BAP years, anxiety and depression scores were below the clinical threshold for significance, for both HIV-infected and affected youth. The prevalent DSM-IV primary diagnoses on Axis 1 across all years were Adjustment Disorder for infected youth and Anxiety Disorder for affected youth.

**Conclusions:** Recent studies have examined the cognitive deficits of perinatally HIV-infected youth, yet few have compared the differences between HIV-infected and affected youths’ cognitive and achievement scores. While both HIV-infected and affected youth could benefit from interventions targeting psychiatric difficulties, family and social relationships, HIV-infected youth have additional problem-solving difficulties that should be addressed. As such, it is likely that HIV-infected youth experience problems negotiating complex medication regimens, making decisions about their academic or career path, and learning budgeting skills. This study suggests the need to provide tailored treatment interventions, targeting the complex mental health and cognitive needs of both HIV-infected and affected youth.
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