Abstract Book
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Abstracts
Oral Presentations
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ARV Treatment of pediatric HIV infection

Virologic Outcomes of Children Switched from Lopinavir/Ritonavir- to Efavirenz-Based Antiretroviral Treatment: a retrospective cohort study


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Introduction: The WHO recommends lopinavir/ ritonavir-based (LPV/r) combination antiretroviral therapy (cART) as first-line for children <36 months old with the option to substitute LPV/r with a non-nucleoside reverse transcriptase inhibitor if virologic suppression is maintained. The NEVEREST-3 randomized controlled trial examined this strategy, showing efavirenz (EFV) to be non-inferior to LPV/r in terms of virologic failure. This simplification strategy is potentially cost-saving, regimen-sparing and more tolerable with fewer long-term side-effects. However, few studies describe outcomes of this practice in routine settings. We aimed to compare outcomes of children commencing cART with LPV/r and substituting it with EFV once virologically suppressed and ≥36 months old (substitution group) with those remaining on LPV/r (stay group).

Materials & Methods: Routine data was collected from 8 South African IeDEA-SA sites. Most sites provide primary- with some providing secondary or tertiary-level care. Sites were eligible for inclusion if they had changed ≥1 virologically-suppressed child from LPV/r to EFV as a single class substitution not due to treatment failure or toxicity. From eligible sites we included all HIV-infected children started on LPV/r-based cART from 2003-2010 who achieved virologic suppression at and had follow-up beyond 36 months of age. None had >1 dose of nevirapine for prevention of mother-to-child transmission of HIV (PMTCT). Logistic regression was used to examine associations between clinically relevant predictors of drug substitution and the probability of having undergone such a substitution. Risk of a viral load (VL) >400 copies/ml after substitution (substitution group) or age 42 months (stay group) was compared using a Cox proportional hazards model adjusted for predictors of virologic non-suppression.

Results: Of 690 children included, 36 underwent substitution at a median age of 44.1 months. Groups were similar at cART start (age, anthropometry, clinical and immunological stage, VL, cART regimen) and at 42 months of age/date of substitution. Experiencing a viral blip (adjusted OR 0.34, 95%CI 0.15; 0.79) and an unfavourable weight-for-age z-score at 36 months (adjusted OR 1.34 per 1 z-score increase, 95%CI 0.96; 1.80) were negatively-associated with substitution. We did not examine associations with PMTCT exposure as this was frequently not recorded. The following clinically relevant variables were associated with time to first VL >400 copies/ml after 42 months of age/substitution: cART duration before 42mo/substitution (adjusted HR 0.96 per extra month on cART, 95%CI 0.93; 0.98, p=0.002), weight-for-age z-score at cART start (adjusted HR 0.87 per 1 z-score increase, 95%CI 0.78; 0.98, p=0.022) and having experienced ≥1 viral blip before 36 months old (adjusted HR 2.26, 95%CI 1.52; 3.36, p<0.001). Having undergone a LPV/r-to-EFV substitution was not associated with time to first VL >400 copies/ml after 42 months of age/ post-substitution in the crude analysis nor when adjusted for the variables above (unadjusted HR 1.03, 95%CI 0.51; 2.11, p=0.923; adjusted HR 1.43, 95%CI 0.62; 3.30, p=0.401)
**Conclusions:** In this cohort, virologic outcomes of children suppressed on LPV/r-based cART and subsequently changed to EFV were no worse than of those remaining on LPV/r. This may be an effective simplification strategy for carefully-selected children without prolonged postnatal nevirapine exposure.

No conflict of interest

**Abstract: 2**

**ARV Treatment of pediatric HIV infection**

The effect of systemic exposure to efavirenz, sex and age on the risk of virological non-suppression in HIV-infected African children.

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**Introduction:** Efavirenz (EFV) is a non-nucleoside reverse transcriptase inhibitor widely used for treatment of HIV-infected adults and children. Despite relatively favourable safety profile the drug exhibits high levels of inter-individual variability in pharmacokinetics (PK) resulting from genetically dependent differences in drug metabolism. Suboptimal drug exposures have been previously related to negative treatment outcomes. The objectives were to describe the effect of systemic EFV exposure on viral suppression, and to derive the minimum exposure predictive of a reduced risk of non-suppression in children participating in the CHAPAS-3 study.

**Materials & Methods:** Individual PK measures (C12h, C24h and AUC) were obtained through population-pharmacokinetic modelling using NONMEM 7.3. Cox multiple failure regression models were used to compute the risks of viral non-suppression (viral load >100 copies/ml) associated with the EFV exposure and other patient factors. Likelihood profiling was utilised to identify most predictive PK cut off-s related to increased risk of a detectable viral load.

**Results:** We analysed 590 matched PK/VL samples from 118 children ages 1.7-13.5 years. The risk of viral non-suppression was best described using a log-linear model which showed a ±40% decrease in the hazard of viral non-suppression for every 2-fold increase in systemic exposure (p<0.001). Graphical representation of the hazard of viral non-suppression, by EFV exposure, using splines, suggested that the decrease in risk of non-suppression plateaued at approximately 8mg/L, 5.65mg/L and 181mg*L/h for C12h, C24h and AUC respectively.

The multivariate analysis identified male gender and older age as other independent risk factors for non-suppression. Children over 8 years old had an increased risk of detectable viral load (p<0.001). Among children under 8years of age, boys had risk of viral non-suppression 5 times higher than girls(p<0.001). The most predictive C12h, C24h and AUC cut-off values for the risk of viral non-suppression for were: 1.2mg/L, 0.65mg/L and 30mg*L/h respectively (all p<0.001). The identified thresholds had relatively high accuracy (>84%) and specificity (>92%) but low sensitivity (33-40%). After adjusting for the effect of sex and age the cut-offs for C12h and AUC remained unchanged but the target for C24h increased to 1.1 mg/L.

**Conclusions:** Our analysis presented a robust approach to establishing the most predictive lower exposure cut-off values related to increased risk of viral non-suppression. Based on these results we suggest mid-dose concentrations of 1.2mg/L and AUC of 30 mg*L/h should be utilised as new paediatric target thresholds. The lower limit for C24h changed after adjusting for sex and age

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suggesting confounding by those covariates. Further studies are warranted to evaluate the association on of treatment adherence with EFV exposure, sex and age.

Conflict of interest: A. Bienczak received a scholarship from EDCTP

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ARV Treatment of pediatric HIV infection

Second-line ART treatment and resistance outcomes of Asian children


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Background: Increasing numbers of children are at risk of failing second-line antiretroviral therapy (ART). With the limitations in pediatric second- and third-line antiretroviral availability in resource-limited settings, data on treatment efficacy and drug resistance following second-line failure are needed to guide regimen sequencing in these settings.

Materials & Methods: HIV-infected children less than 18 years old who were already taking or about to switch to second-line ART after first-line ART failure were enrolled from eight study sites in Indonesia, Thailand, and Vietnam. Clinical and laboratory assessments were retrospectively obtained or prospectively conducted from the time of second-line switch (baseline). Prospective genotyping was performed upon virologic failure (VF; HIV-RNA >1000 copies/mL). Cox proportional hazards regression was used to evaluate factors predicting VF after 6 months post-switch.

Results: A total of 277 children were enrolled; 41% were female. At baseline, median (interquartile range; IQR) age was 7.5 (5.3-10.3) years, median weight was 19.5 (15.5-25.0) kg, median CD4 count was 300 (146-562) cells/mm3, median CD4 percentage was 13 (7-20)%, and median HIV-RNA was 5 (4.4-5.5) log10 copies/mL. The median duration of first-line ART was 2.7 (1.7-4.2) years; 94% were started on non-nucleoside reverse transcriptase (NNRTI)-based regimens. Resistance mutations at first-line ART failure were available in 156 of 277 children, all of whom had been on NNRTI-based regimens. Resistance mutations showed ≥1 thymidine analogue mutation (TAM; 64%), >4 TAMs (18%), Q151M (8%), M184V (82%), K65R (2%), ≥1 NNRTI mutation (92%), and Duet Weight Score >4 (19%). Current second-line regimens contained lamivudine (90%), tenofovir (43%), zidovudine or abacavir (30%), boosted lopinavir (LPV; 91%) and boosted atazanavir (ATV; 7%). After a median of 3.3 (1.8-5.3) years on second-line ART, the median CD4 count was 767 (556-1060) cells/mm3 and median CD4 percentage was 26 (20-31%). Eighteen (7%) had WHO clinical stage 3 or 4 events, and 3 (2%) died from HIV-related illnesses during follow-up. Among the 274 surviving children, VF occurred in 73 (27%) with an incidence of 7 per 100 person-years (95% confidence interval [CI] 5.8-9.1), at which time 23% had less than 95% adherence by pill count and 22% by self-reported visual analogue scale. Resistance mutations in 50 of 73 children with second-line VF included ≥1 TAM (41%), >4 TAMs (10%), Q151M (4%), M184V (55%), at least one major LPV mutation (8%), >6 LPV mutations (2%), and at least one major ATV mutation (4%). Age more than 11 years (hazard ratio [HR] 4.06; 95% CI 2.15-7.66) and HIV-RNA more than 5 log10 copies/mL (HR 2.4; 95% CI 1.27-4.59) at second-line ART switch were significant predictors of VF.
Conclusions: One-fourth of children in this regional cohort had VF while on second-line ART. However, less than 10% developed major mutations to protease inhibitors, which may have been related to intermittent poor adherence and/or limited duration of VF. With the growing numbers of children on second-line ART, greater advocacy is needed to create access to third-line antiretroviral options in resource-limited settings.

No conflict of interest

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ARV Treatment of pediatric HIV infection

Durability of first-line antiretroviral therapy (ART) in children in the European Pregnancy and Paediatric HIV Cohort Collaboration (EPPICC)

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Background: Global data on durability of first-line ART in children is scarce. We assessed time to switch to second-line therapy for any reason in EPPICC (Thailand and 13 European countries including Russia and Ukraine).

Materials & Methods: ART-naive children < 18 years at initiation of combination ART (NNRTI or boosted-PI plus ≥2 NRTIs) were included. Switch to second-line was defined as: (i) change across drug class (PI to NNRTI or vice versa) and change of ≥1 NRTI; (ii) change within PI-class plus ≥1 NRTI; (iii) change from single to dual PI; or (iv) addition of a new drug class. Documented switches for simplification, TB or pregnancy were ignored. Sub hazard ratios (SHR) were estimated from a cause specific hazard model, assessing time to switch and potential predictors, with death as a competing risk. Children were at risk from ART initiation until the earliest of: switch, death, last visit in paediatric care or 21st birthday, with data through to 31st December 2013.

Results: Of 3050 children, 47% were male and 84% perinatally infected. At ART initiation, median [IQR] age was 3.3 years [1.0-8.0], CD4% 20% [13-28] in < 5-years, CD4 count 200 cells/mm3 [55-362] in ≥5-years and 19% were CDC C. Initial regimens were 30% PI-based, 34% NVP-based, 31% EFV-based, and 4% NNRTI+3NRTI. Median duration of follow-up on ART was 5.1 years [2.4-8.0]. Overall, 86 (3%) died, 111 (4%) were lost to follow-up and 684 (22%) met the definition of switch: median time to switch was 28 months [15-57]. 5-year cumulative proportion switching was 22% (95%CI 20-24). Reasons for switch (available in 236 (34%)) were: 69% treatment failure, 14% toxicity, 17% other. 70% of patients with missing reason for switch had viral load (VL)>1000c/ml or CDC B/C event within 6-months prior to switch, varying by regimen (lowest for PIs (46%). In multivariable analysis, older age [SHR (95% CI): 2-4 years 1.25 (0.88, 1.76), 5-9 years 1.95 (1.40, 2.70), 10+ years: 2.35 (1.67, 3.32) compared to < 2 years old; p=0.0001] and higher VL at ART start [SHR (95% CI) per unit increase: 1.16 (1.03, 1.31); p=0.013], UK/Ireland & Rest of European region [SHR (95% CI): Russia and Ukraine 0.51 (0.29, 0.90), Thailand 0.25 (0.18, 0.35), Rest of Europe 0.91 (0.70, 1.19) compared to UK/Ireland; p<0.0001], and initiation on NVP-based or NNRTI+3NRTI regimens [SHR (95% CI): NVP 1.80 (1.38, 2.34), NNRTI+3NRTI 1.71 (1.11, 2.63), PI 0.77 (0.55, 1.06) compared to EFV; p<0.0001] were associated with more rapid time to switch.

Conclusions: Over a fifth of children met the definition of switch by 5-years of ART, with approximately two-thirds likely to be failure related. NVP-based and NNRTI+3NRTI regimens were more likely to switch than EFV or PI-based regimens.

No conflict of interest
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ARV Treatment of pediatric HIV infection

Efavirenz-based therapy may simplify antiretroviral LPV-based therapy initiated in HIV-1-infected children before the age of 2 in West-Africa: the MONOD trial ANRS 12206.

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Background: Early antiretroviral triple therapy initiation in all HIV-infected children <2 years of age (EART) was recommended by WHO in 2010. We hypothesised that an initial EART using a LPV-based therapy could significantly improve their initial virological success. However, in resource-limited settings, LPV-based therapy is rare, usually preserved as a second-line therapy, and had drug interactions with tuberculosis treatment. The MONOD ANRS 12206 trial assessed the question of simplifying ART in HIV-infected children virologically suppressed after 12/15 months on a twice-daily LPV/r based EART initiated <2 years of age with a once daily triple therapy based on efavirenz (EFV).

Materials & Methods: The MONOD ANRS 12026 study is an international, randomized open phase 2-3 non-inferiority trial conducted in Burkina Faso and Côte d’Ivoire (ClinicalTrial.gov registry number: NCT01127204). All HIV-1-infected children (confirmed by DNA PCR), without tuberculosis, receiving <2 years of age a 12-15 month suppressive triple LPV/r based-therapy twice daily together with a cotrimoxazole prophylaxis and therapeutic education, and in virological success (undetectable HIV-ARN <500 copies/mL confirmed) were randomised in two arms: once-daily triple therapy ABC-3TC-EFV (EFV) versus continuation of the initial twice-daily LPV-based regimen (AZT or ABC or 3TC)+LPV/r. The primary analysis was the difference in proportion alive with VL<500 copies/mL (confirmed) by 12-month post-randomisation between arms (14% non-inferiority margin), Chi-square test. Secondary outcomes were safety, clinical and immunological response, adherence, pharmacokinetics, resistance mutation profiles of different regimens and costs.

Results: In the context of low early infant diagnosis coverage (16% in Abidjan; 29% in Ouagadougou), 226 HIV-infected children under 2 years of age were screened between 05/20011 and 01/2013. Among them, 156 (72%) children were included and initiated on EART for 12 months. At 12/15 months on ART, 13 infants have died (8%), 2 were lost-to-follow-up (1%), 3 withdrew (2%), 32 were in virological failure (21%) and 106 (68%) were randomized (54 LPV/r, 52 EFV) with the following characteristics: 44% male, median age 27 months; 77% Abidjan site; 34% of median CD4%, 46% WHO clinical stage 3/4. All were followed up to 12-month: 46 (85.2%) children under LPV vs. 43 (82.7%) under EFV had VL<500 copies/ml by 12-month; difference (2.5%, 95% Confidence Interval (CI) (-11.5, 16.5); 47 (87.0%) under LPV vs. 47 (86.5%) under EFV had VL< 1000 copies/ml; difference 0.5%; 95%CI (-12.4, 13.4). There was no significant difference in severe toxicity: Severe Adverse Events: 3 (5.6%) in LPV vs 4 (7.7%) in EFV arm (p=0.71).

Conclusion: Considering the 1000 copies/mL threshold, the non-inferiority of EFV compared to LPV on VL suppression was shown while we could not conclude to the non-inferiority of EFV using the 500 copies/mL threshold. Resistance analyses are ongoing. This once daily simplified treatment strategy may be interesting in
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ARV Treatment of pediatric HIV infection

Reasons for delayed ART initiation in children with HIV in South Africa

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Background: Rapid initiation of antiretroviral therapy (ART) is critical for achieving good clinical outcomes in HIV+ children. South African national guidelines call for ART for HIV+ children <5years of age with 'fast-track' initiation within 7days for children <12months. For children 5-15years, 2014 guidelines call for ART initiation at CD4+<500. The Pediatric Enhanced Surveillance Study (PESS) is a prospective observational cohort of HIV+ children eligible for ART being conducted at 5 health facilities in Eastern Cape, South Africa. We describe timing of ART initiation and reasons for delay.

Materials & Methods: The PESS study enrolled HIV+ children 0-12years of age in 2012-2014 at the time they were identified as ART eligible by health providers at participating facilities. Children who were alive and on study 3 months after enrollment were evaluated. We examined proportions of eligible children who initiated ART 30, 60 and 90 days after study enrollment, time to ART initiation and reasons children were not started on treatment reported by caregivers and from medical charts. For children <12months we examined the proportion started within 7days among those enrolled after March 2013 fast-track guidance. Chi-square tests were used to compare demographic and clinical factors associated with starting ART.

Results: Among 397 children enrolled, 354 were alive and attending study visits at 3months after enrollment. Median age at study enrollment/ART eligibility was 2.2years (IQR: 7months-8years). At 30, 60 and 90 days after being identified as ART eligible, 270 (76.3%), 297 (83.9%) and 314 (88.7%) children initiated ART, respectively. Only half (50.6%) of the 85 children <12months of age enrolled after March 2013 were started on ART within 7days. Among children starting ART <90days, median time to ART from study enrollment was 8days (range: 0-89). Forty children (11.3%) did not initiate ART <90days of study enrollment: 31 (77.5%) started ART at a median of 119days (range: 91-519) while 9 (12.5%) never started. Among the 40 late starters: 13 children were <=12months and 11 (84.6%) had a viral load >=100,000 copies/mL. Among the late starters >12 months (n=27), 10 (58.8%) had a viral load >=100,000copies/mL and 2 (10.0%) had a CD4+ count <200. The majority of children (47.5%) were delayed from starting ART as a result of the health provider adherence concerns, including lack of treatment supporter or incomplete adherence counseling; other reasons included caregivers not picking up medication (20.0%) and TB treatment (5.0%). The only demographic or clinical factor found to be associated with not starting ART within 90days was having a mother as a primary caregiver (p=0.03).

Conclusions: We found that three-quarters of eligible children were rapidly initiated on ART within 30 days but only half of children <12months started within the 7days per fast-track guidelines. In many cases delayed initiations were a result of perceived adherence challenges, including for younger children and those with high viral load at greatest risk of disease progression and mortality; greater efforts are needed to rapidly initiate children on ART.

No conflict of interest
Abstract

HIV infection and adolescents

Anxiety and depression in young people with perinatal HIV and their HIV-negative siblings

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Background: Few studies have investigated anxiety and depression in perinatally HIV-infected (PHIV+) young people and HIV negative affected controls (HIV-). The role of HIV is unclear with some studies showing increased depression and/or anxiety in both PHIV+ and HIV- young people. We present the first analysis of levels of anxiety and depression in a large UK cohort.

Materials & Methods: We analysed baseline data from the Adolescents and Adults Living with Perinatal HIV (AALPHI) cohort of 290 PHIV+ aged 13-21yrs and 99 HIV- controls (46% siblings of PHIV+, 50% born to a mother with HIV, 4% other) aged 13-23yrs in England. Using computer-assisted interviewing, participants completed the Hospital Anxiety and Depression Scale (HADS) (higher scores = more anxiety/depression), Rosenberg Self-Esteem Scale (RSES) and PedsQL Pediatric Quality of Life (QoL) Inventory. HADS scores were reverse transformed to z-scores (<0=poorer scores compared normative data, >0=better scores) using sex-adjusted normative data for UK young adults aged 25-29yrs (QualLifeRes 2015;24:391-8). T-tests compared means, and linear regression investigated predictors of HADS anxiety and depression scores.

Results: 116(40%) and 30(30%) PHIV+ and HIV- were male, 247(85%) and 72(73%) were black African, median age 16[interquartile range 15,18] and 16[14,18] years respectively. 167(58%) and 46(46%) of PHIV+ and HIV- were not UK born, one/both parents had died in 99(36%) and 22(23%). In PHIV+ 243(86%) were on ART, 182(75%) had VL<50c/ml and median CD4 599mm⁻³ [IQR 410,782] at last visit, 74(19%) had a previous AIDS diagnosis. Mean anxiety scores for PHIV+ and HIV- respectively were 6.4 (SD 3.9) and 6.0 (SD 4.1, p=0.30), 17% and 15% were classified with moderate/severe (score >11). Mean depression scores were 3.9 (SD 3.1) and 3.5 (SD 3.0, p=0.31), 4% and 0% classified as moderate/severe. After adjusting for normative data, mean anxiety z-score in PHIV+ was 0.10 (95%CI -0.03, 0.22) and HIV- was -0.03 (95%CI -0.26, 0.19), and depression PHIV+ 0.07 (95%CI -0.05, 0.19) and HIV- -0.05 (95%CI -0.25, 0.15).

In a multivariable model there was no association between PHIV+ versus HIV- (p=0.87), or gender (p=0.11), and anxiety z-scores. However death of both parents (coefficient -0.47, 95%CI -0.85, -0.09), and ever thinking life not worth living (-0.21, 95%CI -0.3, -0.2) were associated with lower z-scores (higher anxiety). Higher self-esteem (0.05, 95%CI 0.04, 0.07) and higher QoL (0.001, 95%CI 0.001, 0.001) were associated with lower anxiety. For depression, after adjustment, there was no difference for PHIV+ versus HIV- (p=0.650). Death of one (-0.24, 95%CI -0.41, -0.07) or both parents (-0.39, 95%CI -0.78, -0.002) was associated with more depression (lower z-scores). Female sex (0.33, 95%CI 0.16, 0.50), higher self-esteem (0.08, 95%CI 0.06, 0.09) and higher QoL (0.0003, 95%CI 0.001, 0.001) were associated with better z-scores.

Conclusions: No differences were found between PHIV + and HIV- for anxiety or depression scores. Parental death and thinking life was not worth living were associated with poorer scores whilst improved QoL and self-esteem appear protective. Findings suggest that many HIV+ youngsters express feelings of depression and anxiety but levels are similar to HIV- controls and the wider UK population.

No conflict of interest
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Coinfections in HIV infected children

Hepatitis B Treatment Response to TDF in 3TC-experienced Perinatally HIV-infected Adolescents

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Introduction: The risk of progression to chronic liver diseases is high in Hepatitis B (HBV) and HIV coinfection; treatment with tenofovir disoproxil fumarate (TDF) is recommended. This study aims to determine impact of TDF on kinetics of HBV virus, and liver transaminases in lamivudine (3TC)-experienced perinatally HBV-HIV coinfected adolescents.

Materials & Methods: A multi-center prospective cohort of HIV-infected Thai adolescents with HBV coinfection who previously received lamivudine was established. The ARV regimens were modified to add TDF to the ARV regimens. Patients with chronic HBV co-infection were classified into 3 groups according to HBV DNA level: High-level viremia - HBV DNA level > 5.0 log10 copies/mL, Low-level viremia - HBV DNA 2.5-5.0 log10 copies/mL, inactive - HBV DNA < 20 copies/mL. Treatment response of HBV (HBV DNA, HBsAg, HBeAg) and serum alanine aminotransferase (ALT) were measured at 12, 24, and 48 weeks after adding TDF in the regimen. HBV virologic suppression was defined as HBV DNA < 2.5 log10copies/mL (equivalent to 60 IU/mL). The cut-off for normal ALT was <30 IU/mL; ALT > 3xULN was suggestive for presence of liver inflammation, and hepatic flare was defined as ALT >5xULN.

Results: From March 2012 to March 2014, 18 adolescents at median (range) age of 17.6 years(12.9-21.9) were enrolled; 8(44%) were male. Median duration on 3TC exposure was 7.3 years. The mean CD4 lymphocyte count was 632 cells/mm3; 83% had HIV RNA level <40 copies/mL. There are 13(72%), 2(11%) and 3(17%) adolescents who had high-, low-level viremia, and inactive state, respectively. The median (interquartile range) HBV DNA at baseline among 13 adolescents with high-level viremia was 7.73 (7.36-8.10) log10copies/mL. All of 6 cases who get tested had HBV-3TC associated mutations. The median (range) HBV DNA reduction were -2.7(0.6-4.9), -4.6(1.1-6.4), and -5.9(4.7-6.6) log10copies/mL at week 12, 24, and 48, respectively. At week 48 of TDF, 73% achieved HBV virologic suppression, while 27% had low-level persistent viremia. None has HBeAg or HBsAg loss. There were 3 (23%) adolescents who had high baseline ALT (range 34-56 U/L), the ALT was persistently high up to week 48. Among 10 adolescents with normal baseline ALT, only one had transient increase ALT to 3xULN at week 24; none experienced hepatic flare. For the 2 adolescents in low-level viremia group, they have achieved HBV virologic suppression since week 12. For the 3 patients with inactive state, one had HBsAg loss at week 48 without development of anti-HBs.

Conclusions: Using TDF among hepatitis B/HIV co-infected adolescents with 3TC experienced demonstrated high HBV viral suppression at week 48. The response was similar to published data in adults. However, some patients still have persistent elevated ALT.

No conflict of interest
Abstract: 9

HIV infection and adolescents

Prevalence and Associated Factors of Nonalcoholic Fatty Liver Disease and Liver Fibrosis among Perinatally HIV-infected Asian Adolescents

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Background: Liver complications are the important non-AIDS related morbidity in HIV-infected adults. Non-alcoholic fatty liver disease (NAFLD) is a syndrome which may progress toward liver fibrosis and cirrhosis. The study objective was to determine the prevalence and associated factors of NAFLD and liver fibrosis among Asian adolescents with perinatally acquired HIV infection.

Materials & Methods: A case-control study was conducted at 4 pediatric HIV centers in Thailand (Bangkok, Chiang Mai, Khon Kaen) and Indonesia (Jakarta). HIV-infected adolescents aged 10-25 years with virologic suppression and had history of transaminitis within past 12 months were included. Controls were adolescents with normal liver enzymes matched with cases on age and sex. Adolescents with history of hepatitis B/C co-infection or had significant alcohol consumption were excluded. The assessment included liver ultrasonography (USG--for fatty liver; score 1 [mild], score 2 [moderate] and score 3 [severe]), transient elastography (TE--for liver stiffness; TE ≥5.1 kPa – any liver fibrosis, TE ≥7.4 kPa – significant liver fibrosis) and serum liver function test (ALT and AST). Aspartate aminotransferase-to-platelet ratio index (APRI-biomarker of liver fibrosis; >0.5 to 1.5 – mild/moderate, >1.5 – advanced fibrosis) was calculated. NAFLD was defined as evidence of fatty liver and/or significant liver fibrosis. Logistic regression analysis was performed to identify factors associated with the main outcomes.

Results: During August 2014 to March 2015, 51 pairs of case and control were enrolled. Median (IQR) of age and duration of ART were 16.7 (14.6-18.4) and 10.6 (7.1-12.0) years, respectively. Median (IQR) of current CD4 was 740 (594-928) cells/mm3. The prevalence of NAFLD was 18.6%, of which no difference between cases and controls (21.6% vs. 15.7%, p=0.45). Overall, fatty liver by USG was observed in 15 (14.7%) adolescents (mild=13, severe=2). Both adolescents with severe fatty liver were among case group, one had morbid obesity (body mass index=36.2 kg/m2). Thirty-six adolescents (35%) had any liver fibrosis by TE (case=22 [43%] vs. control=14 [27%], p=0.23), whereas significant fibrosis was found in 5 (5%) adolescents, all were cases. APRI biomarker was abnormally high in 3 out of 41 adolescents with any severity of liver fibrosis (TE >5.1 kPa). Sensitivity and specificity of abnormal APRI (>0.5) for prediction of significant liver fibrosis (TE >7.4 kPa) were 40% and 97.7%, respectively. In logistic regression analysis, obesity, CD4 prior to ART initiation, types and duration of ART were not associated with NAFLD in this study. APRI biomarker has low sensitivity to detect hepatic fibrosis. Longitudinal follow-up to monitor for progression and provide appropriate interventions in a timely manner is needed.

Conclusion: About one-fifth of perinatally HIV-infected adolescents met criteria of NAFLD. However, severe fatty liver and significant hepatic fibrosis were more frequent in adolescents with history of transaminitis compared with controls. No significant factor was found to be associated with NAFLD in this study. APRI biomarker has low sensitivity to detect hepatic fibrosis. Longitudinal follow-up to monitor for progression and provide appropriate interventions in a timely manner is needed.

Remark: This study is funded by CIPHER Grants (2014), International AIDS Society

No conflict of interest
Abstract: 10

ARV Treatment of pediatric HIV infection

Week 48 safety and efficacy of a rilpivirine (TMC278)-based regimen in HIV-infected treatment-naive adolescents: PAINT Phase II trial


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Background: Rilpivirine 25mg qd exposure was similar in adults and adolescents (Week 4 PAINT pharmacokinetic analysis). Week 48 safety and efficacy results are reported here.

Materials & Methods: PAINT (NCT00799864) is a Phase II, ongoing, open-label, single-arm trial of rilpivirine plus two investigator-selected N[t]RTIs in treatment-naive HIV-1-infected adolescents (≥12 to <18 years, from sites in India, Thailand, Uganda, South Africa, USA). After the adult approved indication, only patients with viral load (VL) ≤100,000 copies/mL were enrolled. Virologic response was defined as VL <50 copies/mL (time-to-loss-of-virologic-response [TLOVR] algorithm).

Results: Of 36 patients, 20 (56%) were female, 18 (50%) aged 12–<15 years and 32 (89%) Black/African American; 28 (78%) had baseline (BL) VL ≤100,000 copies/mL; 24 (67%) received emtricitabine/tenofovir disoproxyl fumarate (TDF), 8 (22%) lamivudine/TDF and 4 (11%) lamivudine/zidovudine. At Week 48, 26/36 (72%) patients overall, 22/28 (79%) with BLVL ≤100,000 copies/mL and 4/8 (50%) with BLVL >100,000 copies/mL achieved virologic response. Of the ten non-responders (28%), eight were virologic failures (VFs), one was dosed although a protocol violator (screening NNRTI RAM) and withdrawn and one withdrew due to an AE (pulmonary tuberculosis). CD4+ count increased by median (range) 250.5 (-135 to 740) cells/mm3. For 2/8 VFs, overall adherence (pill count) was <95% (one of these also had BLVL >100,000 copies/mL). Five of eight VFs developed rilpivirine RAMs, mostly E138K (n=4), K101E (n=2) and M230L (n=2); 4/5 developed N[t]RTI RAMs, mostly M184V (n=3). Mean (standard deviation) rilpivirine AUC24h and C0h were 2391 (991) ng.h/mL and 84 (39) ng/mL, respectively (population pharmacokinetic analysis). Most AEs were grade 1 or 2. Seven patients (19%) had grade 3 or 4 AEs regardless of causality, mainly malaria and depression (each n=2 and not related to rilpivirine). AEs considered at least possibly related to rilpivirine occurred in 13 (36%) patients, mainly (excluding investigations) somnolence (n=5, 14%) and nausea (n=2, 6%).

Conclusions: This 48-week analysis supports use of rilpivirine 25mg qd combined with other antiretrovirals in treatment-naive HIV-1-infected adolescents (≥12 to <18 years) with VL ≤100,000 copies/mL. Rilpivirine safety, virological and pharmacokinetic results were similar to those observed in adults.

Conflict of interest: JL, TB, JR and FS declare they has no conflicts of interest PF has received grants from Janssen, consultancy fees from Merck and royalties from UpToDate HC, AH, VV and MS are full time employees of Janssen. This study was sponsored by Janssen Pharmaceuticals. Medical writing support was provided by Ian Woolveridge of Zoetic Science, Macclesfield, UK, an Ashfield Company this support was funded by Janssen.
Abstract: 11

Prevention of Mother-to-Child transmission

HIV exposed uninfected South African infants experience greater severity but not frequency of common infectious diseases than HIV unexposed uninfected infants


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Background: 30% of South African children are HIV exposed uninfected (HEU) and experience greater infectious morbidity than HIV unexposed uninfected (HUU) infants. However, this relationship is confounded by social circumstances and breastfeeding differences. The primary objective was to determine whether HEU infants living in similar social circumstances to HUU infants experience greater infectious morbidity after accounting for breastfeeding differences.

Materials & Methods: This prospective cohort study identified HIV-infected and HIV-uninfected mothers and their newborns from a single community midwife unit in 2012/2013. The primary outcome, at least one infectious cause hospitalization or death before 6 months, was determined through active surveillance using the province-wide electronic hospital administration system and mortality registry allowing complete outcome ascertainment. Infectious cause hospitalizations were classified according to modified WHO case-definitions and graded as severe based on WHO danger signs, and very severe based on persistence of danger signs for ≥48 hours. Adjusted odds ratios (aOR) were calculated by multivariable logistic regression. Stratified analyses conditioned on any breastfeeding at 2 weeks and 6 months were performed.

Results: Of 264 mother-infant pairs identified at delivery, 176 (94 HEU, 82 HUU) returned at 2 weeks and continued in follow-up to 6 months. HIV-infected mothers were older (median 27.8 years (interquartile range (IQR) 23.8,31.1) vs. 24.7 (IQR 21.8,29.7), p<0.01) and had lower median delivery CD4 counts (343 cells/mm³ (IQR 23,501) vs. 467 (IQR 363,675), p<0.001) than HIV-uninfected mothers. Maternal education, income and antenatal care were similar, as were household characteristics, mean infant birth weight (3171g (standard deviation (SD) 409g), gestational age (38.91 weeks (SD 1.5)) and immunization up take. At 2 weeks 34% of HEU and 80% of HUU infants were exclusively breastfed, with an equivalent median duration of any breastfeeding (112 days (IQR 56,194)). The incidence rate ratio of all cause sick clinic visits in HEU relative to HUU infants was 0.82 (95% CI 0.58,1.16). Infectious cause hospitalizations occurred in 17 (18%) HEU infants and 9 (11%) HUU infants. One sudden unexplained death occurred in an HUU infant. After adjusting for maternal age and any breastfeeding at 2 weeks (aOR 1.45 (95% CI 0.44,4.55)) or 6 months (1.54 (95% CI 0.60,4.14)) there was no difference in HEU relative to HUU infants for an infectious cause hospitalization (of any severity) or death. The aOR for very severe infectious cause hospitalization or death was 3.12 (95% CI 0.71,14.14). In stratified analysis comparing only infants breastfed at 2 weeks of age, HEU infants had an aOR for a very severe infectious cause hospitalization or death of 5.4 (95% CI 1.20,29.02) compared to HUU infants. Comparing infants with and without an infectious cause hospitalization or death there was no difference in the proportion born to mothers with a CD4 count of <350 cells/mm³ (10/27 (37.0%) vs. 57/149(38.3%), p=0.9).

Conclusion: HEU infants experience a greater severity of infectious morbidity, despite an equivalent frequency of events, similar social circumstances and control for breastfeeding differences. There was no evidence that increased infant infectious morbidity was associated with a low maternal CD4 count in HEU or HUU infants.

No conflict of interest
Abstract: 12

Prevention of Mother-to-Child transmission

Perturbations in gut microbiome in HIV-exposed uninfected (HEU) infants are related to maternal microbiome and human milk oligosaccharides

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Background: Programs to prevent mother-to-child HIV transmission have been highly successful in reducing the risk of HIV transmission to the infant. However, these infants do not escape unscathed. HIV-exposed uninfected (HEU) infants experience higher rates of morbidity and mortality than unexposed infants. Here we investigate a potential mechanism to explain the higher rates of mortality and morbidity in this vulnerable group.

Materials & Methods: Infants born to 25 HIV-infected and 25 uninfected mothers were recruited at a nutrition clinic in Port au Prince, Haiti. All infants were breastfed and the mean age was two months (range one to three months). Mucosal samples were collected from each mother-infant pair (mother: breast milk, areola, vagina; and infant: stool, oral, and skin). For each sample we performed 16S bacterial metagenomic sequencing and analyzed the data using QIIME 1.8.0. Human milk oligosaccharides (HMO) were characterized using high-performance liquid chromatography.

Results: Alpha diversity was significantly reduced in the gut microbiome of infants born to HIV-infected mothers and taxonomic composition differed by maternal HIV status. Specifically, HEU infants had more Proteobacteria and Actinobacteria and less Bacteroidetes and Fusobacteria than infants born to uninfected mothers. Classes within these phyla were also significantly different (Figure). The Bacteroidetes to Firmicutes ratio has been used as a marker of diversity. This link to bacterial diversity was lost in HEUs. Individual mother-infant pairs were significantly similar to each other with the strongest association being between maternal breast milk and infant stool microbiomes. HMO composition of breast milk differed by maternal HIV status. The increases in Proteobacteria and Actinobacteria in HEU infants were explained by increases in the concentration of one of the specific types of HMO, namely 3’ sialyllactose, in breast milk from HIV-infected mothers.

Conclusions: Both HMO composition and infant stool microbiome were influenced by maternal HIV status. Perturbations caused by HIV in the oligosaccharide composition of breast milk or in the maternal microbiome may lead to these perturbations in infants. Close linkage between maternal and infant microbiomes combined with the influence of HIV on HMO may help explain some of the increased vulnerabilities of HEU infants.

No conflict of interest

Abstract: 13

Implementation research on PMTCT and pediatric treatment programs

The impact of adding a virological testing at birth to the existing WHO infant testing algorithm in the 21 Global Plan countries.

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Background: While countries and programs consider providing virological testing at birth (BT) for early identification and initiation of antiretroviral treatment (ART) in HIV exposed and infected infants, uncertainty remains on which settings may benefit the most.

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This comparative scenario exercise seeks to explore efficiency and risk of unnecessarily initiating ART associated with adding BT to the existing World Health Organization (WHO) infant testing algorithm within the 21 Global Plan countries.

Materials & Methods: Four scenarios were defined combining: PMTCT, no-PMTCT, BT, no-BT. Assumptions were developed based on a systematic literature review; specificity and sensitivity of PCR at birth were assumed to be 99% and 100% (for intrauterine infections but 0% for intrapartum infections), respectively. At 6 weeks, the PCR performance was assumed to be 99% sensitivity and 100% specificity (for both intrauterine and intrapartum infections). In the absence of PMTCT, peripartum infections were largely attributed to intrapartum transmission (66%), and if PMTCT was available, then only 33% of peripartum infections were attributed to intrapartum transmission. Each scenario was tested within a population of 5000 HIV-positive women and outcomes of interest were: total number of tests needed, number of tests needed to identify one positive infant, and the number of infants unnecessarily placed on treatment (false positives). For this exercise, 100% uptake of testing and 100% retention in the testing cascade were assumed. The above scenarios were modeled based on HIV transmission estimates (2015-2020) obtained from Spectrum 2015 for the 21 Global Plan countries.

Results: In settings with no PMTCT, the addition of BT was observed to increase the number of tests and the number of tests needed to identify a positive infant (+70% in PMTCT settings vs +90% outside PMTCT). Unnecessary treatment initiations, as a result of false positive tests, were also seen to increase with BT (PMTCT: +68%, No PMTCT: +100%). When applying these scenarios to the 21 global plan countries the proportional increase in number of tests needed was inversely associated with HIV transmission rates. Additionally, the absolute percent increase in unnecessary ARV use in these 21 countries decreased as transmissions rate at 6 weeks increased. The percent increase in tested needed ranged from 80% to 100% as transmission rate decreased from 0.15 to 0.01. The percent increase in the number of children unnecessarily started on treatment increased from 5% at transmission rates of 0.15 to 20% when transmission decreased to 0.01.

Conclusions: Our scenarios exercise suggests that addition of BT in countries with high coverage of PMTCT would be less efficient and could lead to a proportionally higher number of children started on ART unnecessarily compared to countries with low PMTCT coverage. However this is assuming optimal uptake and retention in the testing cascade which suggests that further losses in efficiency may be expected if interventions to improve the testing cascade are not put in place. Re-testing of PCR positives results and active follow up of babies PCR negative at birth appear to be critical across settings. Operational research and cost-effective analyses are urgently needed to fully explore the impact of adding BT to the infant testing algorithm and to target testing approaches to the epidemic setting.

No conflict of interest
Abstract

Background: Novel strategies are needed to increase retention in, and adherence to prevention of mother-to-child HIV transmission (PMTCT) services, and ultimately enhance PMTCT implementation effectiveness in sub-Saharan Africa.

Objective: To determine whether small, increasing cash payments conditioned on attending scheduled clinic visits and receiving proposed services can increase the proportion of HIV-infected pregnant women who attend PMTCT visits and adhere to available PMTCT services through six weeks postpartum.

Materials & Methods: Newly diagnosed HIV-infected women, ≤32 weeks pregnant, were recruited at antenatal care clinics in Kinshasa, Democratic Republic of Congo, and randomly assigned in a 1:1 ratio to an intervention group that received compensation on the condition they attend scheduled clinic visits and accept offered PMTCT services ($5 plus $1 increment at each subsequent visit) or to a control group that received usual care. Outcomes assessed included: retention in care measured by loss-to-follow-up (LTFU), and adherence to PMTCT services (attend all scheduled clinic visits and accept proposed services) through six weeks postpartum. Analysis was by intention to treat. The study is registered with clinicaltrials.gov: NCT01838005.

Results. Between April 2013 and August 2014, 612 potential participants were identified, 545 were screened, and 433 were enrolled and randomized. Participants in the two groups had similar characteristics at baseline. As of January 5, 2015, 407 had completed their six week postpartum visit or were no longer in care. Analysis of complete data showed that by six weeks postpartum, a lower proportion of participants in the intervention group (17.7%) than the control group (27.0%) were LTFU (unadjusted odds ratio (OR), 0.58; 95% confidence interval (CI), 0.36-0.94). Similarly, a higher proportion of participants in the intervention group (70.0%) than the control group (54.5%) attended all scheduled visits and accepted proposed services (OR=1.91; 95% CI, 1.21-2.87). Results were similar after adjusting for marital status, age, and education.

Conclusions: Among newly diagnosed HIV-infected women, small, incremental cash incentives resulted in increased retention along the PMTCT cascade and adherence to available services. The overall effects of these incentives on HIV-free survival and cost-effectiveness warrant further investigation.

Conflict of interest The Study is funded by a grant from the National institute of Health: NIH R01 HD075171

Abstract: 15

Complications of HIV therapy

In utero Tenofovir Exposure is Not Associated with Poor Fetal Long Bone Growth

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Background: Worldwide, there has been a marked increase in tenofovir (TDF) use in pregnant and breast-feeding women since its designation by the WHO in 2013 as part of the first-line Option B+ treatment regimen. However, TDF has been reported to affect bone health in both animal and human studies. Few studies have evaluated in utero TDF exposure and its impact on early fetal long bone growth and development.

Materials & Methods: We evaluated longitudinal fetal long bone measurements via ultrasound from HIV-infected pregnant woman/fetus dyads enrolled in the MCH-ART study in Cape Town, South Africa between 2013 and 2015. Fetal femur (FLZ) and humerus (HLZ) length z scores were calculated. FLZ and HLZ were compared by duration of in utero TDF

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exposure: 1) TDF-exposed since conception (TDF-C) vs. 2) TDF-exposed for >4 weeks and initiated at >14 weeks gestational age (GA) (TDF-E), vs. 3) TDF-exposed for <4 weeks or TDF-unexposed (TDF-U). Pregnancies with multiple gestations or ending in intrauterine fetal demise and ultrasounds performed at <10 weeks GA were excluded. Linear mixed effects models were used to assess the effect of duration of TDF exposure on FLZ and HLZ throughout gestation where TDF exposure was considered a time-varying covariate.

Results: A total of 1957 fetal ultrasounds (408 TDF-C, 581 TDF-E, 968 TDF-U) from 1030 HIV-infected woman/fetus dyads (226 TDF-C, 232 TDF-E, 572 TDF-U) were available for analysis. Median age (31 vs. 27 vs. 28 years, p<0.001) and gravidity (3 vs. 2 vs. 2, p=0.001) of TDF-C women were higher than in TDF-E or TDF-U women. Rates of CD4 cell count < 200 cells/mm³ and log HIV RNA levels at enrollment were higher in TDF-E and TDF-U than in TDF-C women (19.8% and 20.9% vs. 10.1%, p=0.001 and 4.1 and 4.0 vs. 1.6, p<0.001 respectively). Median GA at first ultrasound, socioeconomic status, rates of previous low birth weight (< 2500g) infants, and maternal height and body mass index (BMI) did not differ between groups. Median weeks on TDF prior to each ultrasound observation were: 26.9 (Interquartile Range [IQR]:19.6-33.7), 13.0 (IQR: 9.6-17.6), and 0.0 (IQR: 0-0.2) amongst TDF-C, TDF-E and TDF-U groups respectively. Mean FLZ and HLZ did not differ by exposure to TDF (0.321 vs. 0.300 vs. 0.333, p=0.570 and 0.130 vs. 0.318 vs. 0.048, p=0.832 respectively). These relationships persisted even after adjusting for maternal age, gestational age, gravidity, socioeconomic status, CD4 cell count, HIV RNA level, and maternal BMI (β=0.038, p=0.563 for TDF-C vs. TDF-U and β=0.002, p=0.964 for TDF-E vs. TDF-U fetal FLZ; β=0.009, p=0.903 for TDF-C vs. TDF-U and β= 0.006, p=0.885 for TDF-E vs. TDF-U fetal HLZ).

Conclusions: In utero TDF exposure does not appear to alter fetal long bone growth. These results are re-assuring and support the continued use of TDF in HIV-infected pregnant women.

No conflict of interest

Abstract: 16

Prevention of Mother-to-Child transmission

Psychosocial factors in younger versus older HIV-infected pregnant women initiating antiretroviral therapy in Cape Town, South Africa

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Background: HIV-infected pregnant women living in sub-Saharan Africa are at high risk for alcohol abuse, depression, and violence; young adult women in particular may be more vulnerable. However, little is known about the psychosocial context of this population.

Materials & Methods: We compared younger (18-25 years of age) and older (>25 years of age) HIV-infected pregnant women initiating antiretroviral treatment (ART) in antenatal (ANC) services in Cape Town, South Africa between March 2013 and June 2014. Consecutive women were assessed by trained interviewers on a range of psychosocial measures, including the Edinburgh Postnatal Depression Scale (EPDS), the Alcohol Use Disorders Identification Test (AUDIT), self-reported Perceived Availability of Social Support, and HIV Social Impact Scale. Measures were compared using Chi-squared, Fisher’s exact, Wilcoxon, t-tests, and logistic regression.

Results: Among 626 women initiating ART (mean age 28 years), younger women were more likely to be diagnosed with HIV during the current pregnancy (69% vs 48%, p<0.001). During the current pregnancy, 14% were at moderate-high risk of harmful alcohol use, and
22% had experienced alcohol-related harm (e.g. memory loss, injury to self or others due to alcohol use); these were similar across both groups. In a subgroup analysis stratifying the younger women by age, 37% of 18-21 year-olds had experienced alcohol-related harm (p=0.002). Overall, 20% of women were at risk for depression on the EPDS. Younger women had a higher risk of depression compared to older women (24% vs 17%, respectively, p=0.048). Reports of self-harming thoughts in the previous seven days were significantly higher in younger (10%) vs older (4%) women (p=0.001). Depression risk and self-harming thoughts remained significantly higher in younger women after accounting for timing of HIV diagnosis. There were no differences between the two groups in pregnancy intentions, social support, or social impact of HIV.

Conclusions: Young HIV-infected pregnant women have increased risk of depression and levels of self-harming thoughts, with particularly high levels of alcohol-related harm among the youngest women. Given the impact of depression and alcohol abuse on HIV treatment and pregnancy outcomes, these data point to the need for interventions targeting this highly vulnerable population.

No conflict of interest

Abstract: 17

Comprehensive Pediatric HIV care

Hearing Loss in HIV-Infected Children in Lilongwe, Malawi

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Introduction: With improved access to pediatric antiretroviral therapy (ART), HIV infection has become a chronic illness. Preliminary data suggest that HIV-infected children have a higher risk of disabilities such as hearing impairment. This study aimed to estimate the prevalence and types of hearing loss in HIV-infected children in Lilongwe, Malawi.

Materials & Methods: This was a cross-sectional survey of 380 HIV-infected children aged 4-14 years attending ART clinic in Lilongwe from December 2013-March 2014. Data was collected through pediatric quality of life (PedSQL™) and sociodemographic questionnaires that were translated into Chichewa and reviewed with a research assistant, review of the electronic medical record, and audiologic testing for all participants. Hearing loss was defined as hearing loss >20 dB in either ear. Predictors of hearing loss were explored by multiple regression analysis generating age- and sex-adjusted odds ratios. Children with significant hearing impairment were fitted with hearing aids.

Results: Of the 380 recruited patients, 90 (24%) of patients had hearing loss in either ear. 82% of the hearing loss was conductive, 14% was sensorineural, and 3% was mixed. Twenty-one patients (23% of those with hearing loss) were referred by audiologists for hearing aid fitting. There was a higher prevalence of hearing impairment in children with history of frequent ear infections (OR 7.4, 4.2-13.0) and ear drainage (OR 6.4, 3.6-11.6). Hearing impairment was linked to history of WHO Stage 3 (OR 2.4, 1.2-4.5) or Stage 4 (OR 6.4, 2.7-15.2) and history of malnutrition (OR 2.1, 1.3-3.5), but not to duration of ART or measures of CD4. Only 40% of caregivers accurately perceived that their child had hearing loss. Children with hearing impairment were less likely to attend school and had poorer emotional (p= 0.02) and school functioning (p = 0.04).

Conclusions: Hearing impairment was common among children with HIV, and can affect school functioning and quality of life. Many children with hearing loss qualified for hearing aids. Caregivers were not reliable at identifying hearing loss. There is therefore an urgent need for improved screening and identification of hearing problems in HIV-infected children to treat this disability, especially in resource-limited settings.

No conflict of interest
Abstract: 18

Coinfections in HIV infected children

Lower immune response in HIV-positive girls to the quadrivalent human papillomavirus vaccine

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Background: The quadrivalent human papillomavirus vaccine (qHPV) is approved for use in HIV-negative (HIV-) adolescents and leads to high rates of seroconversion. There is limited information on the immune response in HIV-positive (HIV+) girls/adolescents.

Materials & Methods: Participants were given 3 doses of qHPV at months 0, 2 and 6. Antibody levels to HPV 6, 11, 16, 18 were measured pre-vaccine and post-vaccine at months 7, 12, 18 and 24 by the Merck cLIA assay. HIV- girls of the same age who received 3 doses of qHPV vaccine in a separate study* (N=261) served as controls. Post-vaccination geometric mean titers (GMT) of HIV+ and HIV- girls were compared. Seroconversion was defined as achieving serotype-specific cut-offs for positivity of 20, 16, 20, and 24 mMU/mL for HPV 6, 11, 16, and 18, respectively.

Results: Of a total 407 HIV+ study subjects, 32 girls aged 9-13 years were enrolled and vaccinated. All completed the vaccine schedule per protocol. One was seropositive to HPV 18 at baseline; all others were seronegative to all 4 vaccine serotypes. Mean age was 11 years, 81% were black, 3% white and 16% other. Median (IQR) baseline CD4 was 692 cells/mL (547-929); CD4 nadir was 442 cells/mL (246-594). Viral load was undetectable (<40 copies/mL) in 59%. All girls had seroconverted at month 7, but by month 24 seroconversion rates were 86%, 81%, 100%, and 70% to HPV 6, 11, 16, and 18, respectively. GMTs for all 4 serotypes were significantly lower in HIV+ compared to HIV- girls at both 7 months [serotype 6 (844 vs 1856, p<0.0001), 11 (971 vs 2096, p<0.0001), 16 (4924 vs 7640, p<0.01), 18 (703 vs 1703, p<0.001)] and 24 months [serotype 6 (122 vs 359, p<0.0001), 11 (114 vs 422, p<0.0001), 16 (688 vs 1739, p<0.0001), 18 (71 vs 267, p<0.001)]. Among HIV+ girls, GMT was 2-3 times higher at month 7 and 2-6 times higher at month 24 in those with versus those without virologic suppression at time of first vaccination. However, when compared to the HIV- controls, GMTs in the HIV+ girls with virologic suppression were still significantly lower for all HPV types at months 7 and 24 with the exception of HPV 16 at month 7 (p=0.21) and HPV 6 at month 24 (P=0.06).

Conclusion: A statistically significant lower peak GMT and a more rapid antibody decline was observed in HIV+ girls compared to HIV- girls of the same age. Ongoing monitoring of the efficacy and effectiveness of qHPV in this population is needed.

No conflict of interest

Abstract: 19

HIV infection and adolescents

Changes in renal laboratory parameters and bone mineral density in treatment-naïve HIV-1-infected adolescents initiating E/C/F/TAF or E/C/F/TDF

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Reviews in Antiviral Therapy & Infectious Diseases 2015_8
Abstract: 20

Complications of HIV therapy

Decreased bone mass in perinatally HIV-infected school-aged South African children on antiretrovirals

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Introduction: Decreased bone mineral content (BMC) and bone mineral density (BMD) by dual-energy X-ray absorptiometry (DXA) have been described in children with HIV-infection. However, no studies have been conducted in resource-limited settings, where >90% of HIV-infected youth now live.

Materials & Methods: We present baseline results of the bone sub-study of CHANGES, a prospective, two-year observational cohort study of 220 HIV+ and 180 HIV- pre-pubertal South African children who initiated ART before age 2. Weight- (WAZ) and height- (HAZ) Z-scores were calculated using WHO standards and CD4 and HIV-RNA levels were measured. BMC and BMD of the whole body (WB) and median increase in spine mineralization. Both STRs were well-tolerated through 24 weeks. These findings support INSTI-based STRs as initial HIV-1 treatment in adolescents and suggest that TAF could offer safety advantages in pediatric populations.

Conflict of interest: S Bennett, Y Shao, and E Quirk are employees of Gilead Sciences.

Abstract: 20

Complications of HIV therapy

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lumbar spine (LS, L1-4) by DXA were assessed using a Hologic Discovery W densitometer (Hologic Inc, Bedford, MA). Reference curves from the BMD in Childhood Study were used to generate Z-scores for WB and LS BMC (Kalkwarf 2007). All measures were compared between groups by t-tests and chi-squared tests.

Results: 220 HIV+ children (49% male) and 180 HIV- children (55% male) were included. HIV+ children were younger than controls (mean age 6.4 vs. 7.1 years, p<0.01). All HIV+ children were on antiretroviral therapy (ART), started at a mean of 8.9 months of age (48% started before 6 months). Half were on a protease inhibitor (PI)-based regimen (100% ritonavir-boosted lopinavir) and half were on a non-nucleoside reverse transcriptase inhibitor (NNRTI)-based regimen (99% efavirenz), both in combination with two nucleoside reverse transcriptase inhibitors, including lamivudine and abacavir or stavudine, but not tenofovir. 93% had HIV-RNA <400 copies/mL at the time of evaluation. Mean CD4% was 37.3. HIV+ children had lower mean WAZ (-0.82 ± 0.9 vs -0.58 ± 1.0, p=0.01) and HAZ (-1.37 ± 0.9 vs -1.18 ± 1.0, p=0.046) than HIV- children. WB BMC (416 ± 98 vs. 496 ± 123, p<0.01) and BMD (0.51 ± 0.06 vs. 0.56 ± 0.07, p<0.01) were lower in HIV+ compared to HIV- children, and the difference remained significant after adjustment for weight and height. Similarly, LS BMC (14.5 ± 3.1 vs. 16.1 ± 3.4, p<0.01) and BMD (0.46 ± 0.06 vs. 0.49 ± 0.07, p<0.01) were lower in HIV+ compared to HIV- children, but not after adjustment for weight and height. Similar patterns were observed with WB (-3.32 ± 1.8 vs. -2.06 ± 1.6, p<0.01) and LS (-2.18 ± 1.6 vs. -1.59 ± 1.3, p<0.01) BMC Z-score. When analysis was limited to 60 HIV+ and 54 HIV- children with normal growth (WAZ and HAZ between -1 and 1), WB BMC, WB BMD, LS BMC and LS BMD remained lower in the HIV+ group.

Conclusions: Despite early initiation of ART and excellent virologic control, in this sample of South African school-aged children, HIV+ children receiving ART have lower indices of bone quality by DXA compared to HIV- controls. Differences cannot entirely be accounted for by smaller body size alone.

No conflict of interest

Abstract: 21

Complications of HIV therapy

Early cardio-pulmonary disease in children despite early ART - Evidence from CHER cohort

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Background: Untreated HIV infection in children is associated with chronic progressive pulmonary and vascular disease. The degree to which early antiretroviral therapy (ART) prevents this is unclear. Maximal oxygen consumption (VO2max) is the gold standard measure of cardiovascular and respiratory fitness and a sensitive marker of early cardiovascular or respiratory disease.

Materials & Methods: In 125 children (77 HIV-infected; 48 uninfected), we performed a standardized 3-minute step test to estimate VO2max using a previously validated formula for healthy children aged 8-12 years. The HIV-infected children had initiated ART (lopinavir/r, lamivudine, zidovudine) in infancy at median 9.1 (interquartile range, IQR: 7.4 - 11.8) weeks of age. We measured fasting lipids, along with fat-free body weight and vertebral bone mineral density (BMD) using dual energy X-ray absorptiometry (DXA). Vertebral BMD z-score for age and gender was used as a surrogate marker of chronic malnutrition, and fasted total cholesterol as a surrogate for high trans-fat / high refined carbohydrate diet, which are common in our local population. Estimated VO2max was corrected for fat-free body weight before being entered into a multivariate linear regression as the dependent variable.
Results:

Table 1: Description of participants

<table>
<thead>
<tr>
<th>HIV-infected, N=77</th>
<th>Uninfected, N=48</th>
<th>Univariate p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (median, range) (years)</td>
<td>7.7 (7.4 - 8.7)</td>
<td>8.5 (7.4 - 8.8)</td>
</tr>
<tr>
<td>Gender (male/female)</td>
<td>44% / 56%</td>
<td>63% / 38%</td>
</tr>
<tr>
<td>Body mass index</td>
<td>16.2 (12.2 - 20.2)</td>
<td>17.0 (11.5 - 22.4)</td>
</tr>
<tr>
<td>Fat-free body mass (kg)</td>
<td>17.6 (13.0 - 22.3)</td>
<td>18.9 (13.7 - 24.2)</td>
</tr>
<tr>
<td>Unadjusted VO$_2$max (ml/min/kg)</td>
<td>33.6 (23.4 - 43.9)</td>
<td>35.6 (21.0 - 51.1)</td>
</tr>
<tr>
<td>Vertebral BMD z-score</td>
<td>-0.5 (-2.5 - +1.6)</td>
<td>-0.2 (-2.1 - +1.7)</td>
</tr>
<tr>
<td>Total cholesterol (mmol/L)</td>
<td>4.2 (2.7 - 5.7)</td>
<td>3.5 (2.1 - 5.0)</td>
</tr>
<tr>
<td>Triglyceride-HDL ratio (median, IQR)</td>
<td>0.7 (0.5 - 1.0)</td>
<td>0.4 (0.3 - 0.7)</td>
</tr>
</tbody>
</table>

Variables are presented as mean (95% confidence interval) unless otherwise stated. IQR = Interquartile range; BMD = bone mineral density

On univariate analysis, VO$_2$max was similar in HIV infected and uninfected children (p=0.11). However, after adjustment for vertebral BMD z-score, total cholesterol, age and gender, HIV-infected children had a significantly lower VO$_2$max per kg fat-free body weight (p=0.03).

Conclusions: While early ART offers substantial benefit, it may not entirely prevent chronic non-infectious pulmonary and cardiovascular disease in perinatally-infected children.

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Computerized cognitive rehabilitation training can improve neuropsychological outcomes in rural school-age Ugandan children with HIV.

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Introduction: Millions of children worldwide with HIV are at risk for neurocognitive disorders due to HIV encephalopathy. Even clinically stable children can have neuromotor, attention, memory, visual-spatial, and other executive function impairments. This study is the first to evaluate the neuropsychological benefits of computerized cognitive rehabilitation training (CCRT) training in African children with HIV, who have had little prior exposure to computers.

Materials & Methods: 159 rural Ugandan children with WHO Stage I or II HIV disease (6 to 12 years; 77 boys, 82 girls; M=8.9, SD=1.86 yrs) were randomly assigned to one of three treatment arms over a two-month period. The CCRT arm received 24 one-hour sessions (3 days per week) using Captain’s Log (BrainTrain Corporation) programmed for nine different games selected through prior screening to be appropriate for children in this cultural context. The games targeted working memory, attention, and visual-spatial analysis, with each game becoming increasing more difficult as the child gained mastery. The 2³rd arm was a ‘limited CCRT’ with the same nine games rotated randomly through the simplest levels of training. The third arm was a passive control group receiving no computer training. All children were assessed at enrollment prior to training, 2 months later (post-CCRT), and 3 months following the end of the training. Every training session was supervised by a research assistant.

No conflict of interest
and occurred in a quiet room in or near the child’s home. In addition to Captain’s Log program-based measures of performance improvement to ensure fidelity of training, assessment outcomes included the Kaufman Assessment Battery for Children, 2nd ed. (KABC-II), the CogState computerized cognitive performance test, Tests of Variables of Attention (TOVA), Behavior Rating Inventory of Executive Function (BRIEF; parent version), and the Achenbach Child Behavior Checklist (CBCL, parent version).

Results: At post-training and 3-mo follow-up, the CCRT group had significantly greater gains compared to passive controls on overall KABC-II performance ($P<0.01$), Planning/Reasoning ($P=0.04$), and Knowledge ($P=0.03$). The limited CCRT group performed better than controls on Learning ($P=0.05$). Both CCRT arms had significantly greater gains on CogState Groton maze learning ($P<0.01$), but not any of the other CogState memory or attention measures, TOVA attention/impulsivity, or BRIEF and CBCL behavior/symptom ratings. Compared to controls, global performance gains on KABC-II and CogState were significant for both the CCRT and CCRT-limited children who were on HAART ($P<0.02$). CCRT gains in KABC-II, CogState, and TOVA performance during training were significantly associated with Captain’s Log performance improvements of training fidelity across the 24 training sessions ($P<0.01$).

Conclusions: CCRT intervention can be an effective and viable means of neurocognitive rehabilitation in children with HIV in low resource settings. We are evaluating whether neurocognitive gains correspond to gains in academic achievement, or improvements in behavioral adjustment in the home or community. These are important considerations as more evidence emerges regarding the behavioral and psychosocial risk to children with HIV in low-resource settings as they survive into adolescence. Future studies are planned evaluating cognitive games for tablets and smart phones that can make cognitive evaluation and CCRT accessible on a mobile network.

No conflict of interest
month of TB/HIV therapy (PK2) and 2-4 weeks after stopping TB therapy (PK3).

PK1 contributed to the development of a structural model of LPV PK. This model was then used to predict $C_{0\text{morning trough}}$ LPV levels at PK2 and at PK3. We compared the percentage of children with model-predicted $C_{0\text{morning trough}}$ below 1 mg/L at PK2 and PK3 for non-inferiority, with non-inferiority threshold set at 10% points. We present an interim analysis conducted in May 2015.

**Results:** In this analysis, 80 of 89 recruited participants contributed to the PK data. At enrolment, median age and weight were 19.1 months and 8.8 kg, 33% of the children were below 12 months of age, 39% WHO clinical stage 3 and 61% stage 4, with median CD4 percent 16%. TB therapy was started first in 66 (74%) children.

The observed median $C_{0\text{morning trough}}$ at PK1 was 5.95 mg/l (Interquartile range 2.82-9.05) at PK2 7.0 mg/l (2.26-10.5) and PK3 8.85 mg/l (4.4-12.7). The percentage of modelled morning trough levels below target upon super-boosting was 10.7% (CI 3.3% to 19.6%) and off TB therapy was 15% (CI 5.1%-27.7%). The median value of the difference between the modelled morning troughs below the 1 mg/L threshold was -4.4% (95% CI -12.1% to 1.4%), confirming the non-inferiority of LPV exposure upon superboosting LPV/r (1:1) over standard regimen LPV/r (4:1).

24 Serious adverse events (SAEs) including 3 deaths occurred. The deaths were unrelated to study treatments. One case of jaundice and elevated liver enzymes was reported. Although treatment was interrupted, this was not thought associated with study therapy. Viral load <1000 copies/ml was achieved after 6 months of superboosted ART and TB therapy in 80% of children. No major protease resistance mutation was reported in children not suppressing.

**Conclusions:** Super-boosting is a safe and effective for TB/HIV co-infected children.
7th International Workshop on HIV Pediatrics

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Abstracts
Poster Presentations
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ARV Treatment of pediatric HIV infection

Second and third line antiretroviral therapy options for children and adolescents: a systematic review

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Background: The World Health Organization (WHO) recommends switching to a boosted lopinavir (LPVr) based 2nd line regimen after failing a 1st line non-nucleoside reverse transcriptase inhibitor (NNRTI) regimen and to a NNRTI-based regimen for LPVr-based failure. Those subsequently failing 2nd line antiretroviral therapy (ART) require tailored 3rd line regimens. This review aimed to identify evidence to support 2nd and 3rd line ART choices for HIV-infected children failing 1st and 2nd line ART respectively.

Materials and methods: For published studies we comprehensively searched, without language or date limitations, the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, and EMBASE. For unpublished and ongoing studies we screened abstracts from relevant conference proceedings up to and including February 2015 and searched the WHO International Clinical Trials Registry Platform and ClinicalTrials.gov. Two reviewers independently screened abstracts and titles for eligibility. Data were abstracted independently using a standardized data extraction tool. Risk of bias (ROB) was assessed using Cochrane Collaboration tool for randomized control trial (RCTs) and the Newcastle Ottawa Scale for Phase II trials and observational studies. Studies only reporting on 1st line therapy (ART naïve) outcomes and those that did not include outcomes for children below 19 years were excluded. The primary outcome of review was the proportion of patients achieving viral suppression as defined by the individual study.

Results: The search retrieved 1979 records. We examined the full text of 53 articles. Twenty-five studies met eligibility criteria. Five studies examined drugs no longer considered suitable for paediatric use: Tipranavir, maraviroc and enfuvirtide. Only one RCT was identified, assessing tenofovir disoproxil as add-on therapy to a failing 1st line regimen but not as part of a new 2nd line regimen.

The remaining 19 studies (seven Phase II, three prospective cohorts, nine retrospective cohorts) included 1085 children and adolescents with a median sample size of 49, IQR 21-110. Seven evaluated regimens in children needing 2nd line therapy (c-SEC), five in children needing 3rd line therapy (c-THD) and eight included children who were in need of 2nd OR 3rd line treatment (c-SEC-THD). Regimens evaluated were 1.) c-SEC: Efavirenz (EFV); LPVr; atazanavir (ATVr); and various combinations of LPVr, ATVr, indinavir, saquinavir, and nelfinavir 2.) c-THD: LPVr; Etravirine (ETV); Darunavir (DRVr) plus raltegravir (RTG); DRVr plus RTG with ETV; and various combinations of DRVr, RTG and ETV 3.) c-SEC-THD: ATVr; DRVr; ETV; RTG, dolutegravir and elvitegravir. On average, 71% of c-SEC; 49% of c-THD and 53% of c-SEC-THD were virally suppressed at 1 year (Week 48/Month 12). No study compared currently recommended LPVr-based second line regimens for NNRTI-failures to other non-NNRTI regimens head-to-head. All 19 studies were judged to have high risk of bias.

Conclusions: There is insufficient evidence to directly evaluate alternative 2nd and 3rd line ART options for children. Current recommendations are still based on inference from adult trials. Well-designed RCTs across age ranges and prior ART regimens are urgently needed.

No conflict of interest
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ARV Treatment of pediatric HIV infection

Initial findings from IMPAACT P1104s: a neuropsychological evaluation of HIV-infected and uninfected children in sub-Saharan Africa


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Background: Children with perinatal HIV infection are at-risk for neuropsychological deficits, but few studies have performed neuropsychological evaluation of children across multiple sites in resource-poor settings. Principal aims are: 1) Establish the feasibility of administering a neuropsychological battery in perinatally HIV-infected (HIV), HIV-uninfected perinatally-exposed (HEU) and HIV unexposed (HU) children across 6 sub-Saharan sites; 2) Compare initial neuropsychological outcomes among HIV, HEU, and HU children across sites.

Materials & Methods: IMPAACT P1060 compared Nevirapine- versus Lopinavir/Ritonavir-initiated ART in HIV children 6 to 35 months of age. P1104s evaluates their cross-sectional and longitudinal neurocognitive performance over two years from 5 to 11 years of age, compared to age-matched HEU and HU controls using the Kaufman Assessment Battery for Children, 2nd edition (KABC-II); computerized Tests of Variables of Attention (TOVA); Bruininks-Oseretsky Test of Motor Proficiency, 2nd edition (BOT-2); and the Behavior Rating Inventory of Executive Function (BRIEF; completed by the caregiver in the local language). Exposure groups are compared using both the Kruskal-Wallis test and least-squares means adjusted for site, age and gender. The HIV treatment-arm comparisons are made using an unadjusted Wilcoxon rank-sum test.

Results: 615 participants were enrolled (mean age 7.2 ± 1.4, 47% boys) at 6 sites (South Africa (3), Zimbabwe, Malawi, Uganda). Accrual goals were met within 14 months, enrolling 246/248 (99%) of P1104s/P1060 eligible children, 185 age-matched HEU, and 184 age-matched HU children. Between 91.5-95.6% of the cohort children completed all three tests (KABC-II, TOVA, BOT-2) in one day with high overall completion rates (TOVA 95-98%; BOT-2 and KABC close to 100%), and only 3% being invalid (KABC by cohort). Three of the enrolled HIV infected children were untestable with profound neurodisability. The three cohorts (HIV, HEU, HU) differed on KABC-II Mental Processing and Nonverbal Indexes, TOVA attention and impulsivity, BOT-2 total motor proficiency (P<0.001), but not on the BRIEF. The HIV cohort performed significantly worse than the HEU and HU cohorts. The HU consistently performed better than the HEU cohort, but the adjusted differences were not significant when combined across sites. There were significant site-by-cohort interaction effects for the KABC-II and TOVA global performance measures (P<0.01), indicating that the magnitude of the performance differences among the three cohorts varied across sites. There were no differences in neuropsychology outcomes among the HIV+ cohorts treated with either NVP or Lopinavir/Ritonavir (intent to treat).

Conclusions: We establish the feasibility of obtaining multi-site neuropsychological measures in African children with HIV along with appropriate control comparisons; with significant performance deficits for the HIV group across all 6 sites despite language and cultural differences. Still, the significant group-by-site interaction effects for cognitive test outcomes evidence the importance of...
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ARV Treatment of pediatric HIV infection

A Pharmacokinetics-Based Adherence Measure for Antiretroviral Therapy in HIV-Infected Kenyan Children

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Background: Traditional medication adherence measures do not accommodate the pharmacokinetic (PK) properties of the drugs and thus do not reflect patients’ true therapeutic exposure. Medication Event Monitoring Systems (MEMS®) dose timers coupled with established PK parameters offer an opportunity to quantify the proximity of patient’s actual drug exposure to its intended level. We tested the concept by constructing a PK-based measure for Nevirapine (NVP) adherence in HIV-infected Kenyan children.

Materials & Methods: We used a 1-compartment model with previously established PK parameters and actual MEMS®-recorded dosing times to estimate the mean plasma concentration of NVP (Cp) in individual patients after 1 month of follow-up. Intended NVP plasma concentration was calculated given a perfectly followed dosing regimen and frequency (Cp'). The difference and the ratio between the two (Δ=Cp'-Cp and R=Cp/Cp') quantified the extent to which the patient’s NVP actual exposure deviated from its intended level. A larger Δ value suggests greater deviation of the observed plasma concentration from the intended level. Similarly, an R value much less than 1 indicates poor adherence. We validated Δ and R by evaluating its associations with MEMS®-defined adherence, CD4%, and spot-check NVP plasma concentrations assessed after 1 month.

Results: We analyzed data from 152 children (84 female). Mean age was 7.9 years (range 1.5–14.9). Subjects were on NVP for an average of 2.2 years. Children had moderate to severe clinical disease (61.7% were at WHO Stages 3 or 4) with mean CD4% of 27.7%. Mean MEMS® adherence was 78.6%. The mean Δ and R values were -0.04 ng/ml (SD 0.16 ng/ml) and 1.11 (SD 0.37), respectively. Δ was negatively associated with MEMS® adherence; patients with MEMS® adherence ≥ 90% had mean Δ value of -0.11 ng/ml versus mean Δ of 0.02 ng/ml in those with MEMS® adherence < 90% (p<0.0001), confirming a larger Δ was associated with non-adherence and thus a greater deviation from the intended level. A larger Δ was also associated with lower CD4% (p=0.0238) and spot-check plasma concentration (p=0.0008). R was positively associated with MEMS® adherence (r=0.506; p<0.0001). The mean R value was greater in patients with MEMS® adherence ≥ 90% than those with lower MEMS® adherence (1.26 vs 1.00; p=0.0001). A larger R value was associated with higher CD4% (p=0.0447) and spot-check plasma concentration (p=0.0090).

Conclusions: The proposed adherence measures, Δ and R, captured patient drug-taking behaviors in addition to the PK properties of NVP; these measures’ associations with MEMS®, CD4%, and spot-check plasma concentration confirmed their validity.

No conflict of interest
Abstract

ARV Treatment of pediatric HIV infection

Addressing barriers to managing treatment failure and advanced ART for children and adolescents: informing health system strengthening through the New Horizons initiative

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Background: Programmatic scale-up in response to recent fast-track global HIV treatment targets is intended to significantly increase the number of HIV-infected children and adolescents initiated on ART. As this number rises, an increase in prevalence of treatment-experienced HIV among children and adolescents is also to be expected. In 2014, the New Horizons (NH) Advancing Pediatric HIV Care initiative was launched by Janssen Pharmaceuticals in collaboration with the Elizabeth Glaser Pediatric AIDS Foundation (EGPAF), and Partnership for Supply Chain Management (PFSCM). Built from a core pediatric darunavir/etravirine Donation Program, NH aims to create a framework for health systems strengthening to support national HIV/AIDS programs in the management of children and adolescents with treatment-experienced HIV. The objective of the current analysis is to identify major gaps and barriers to inform the design of ongoing and future NH health systems strengthening activities for national-level HIV/AIDS programs.

Materials & Methods: In November 2014, representatives from each national HIV/AIDS program engaged in the NH Donation Program were invited to attend a workshop in Johannesburg, South Africa focused on advanced pediatric HIV treatment. Gaps and barriers to the management of ART for children and adolescents with treatment-experienced HIV were systematically documented during interactive sessions with workshop participants. Information to support the analysis was also abstracted from national guidelines and other submitted materials.

Results: Three national HIV/AIDS programs (Zambia, Kenya and Swaziland, as well as clinical experts from South Africa) participated in the first NH workshop and shared their countries’ pediatric/adolescent second- and third-line ART guidelines. Each program also described provisions for the management of pediatric and adolescent HIV/AIDS support services as well as perceived gaps and barriers to the management of advanced treatment for these cohorts. The major gaps and barriers identified were: a) limited systematic data collection regarding pediatric and adolescent ART failure; b) limited expertise in the management of second- and third-ART for children and adolescents; c) limited capacity to provide resistance testing (i.e., weak diagnostic infrastructure, lack of expertise, etc.); and challenges to retaining adolescents in care. The barriers to adolescent retention identified by NH workshop participants included disclosure challenges (parent to adolescent, adolescent to parent, adolescent to external social network, etc.); attendance of boarding schools by HIV infected adolescents; limited health care workforce (HCW) capacity to provide adherence support to adolescents and their families; limited number of adolescent friendly facilities; and challenges in the transition to adult care.

Conclusion: Informed by the analysis of cross-cutting and country-specific barriers, the NH collaborative has designed specific health systems strengthening activities including: a) capacity building materials for pediatric HIV healthcare providers regarding adolescent support services, identification and management of ART failure, adherence support and evaluation of resistance, etc.; b) facilitated peer-to-peer knowledge exchange to increase pediatric and adolescent care and treatment expertise; and c) a pediatric HIV cohort monitoring system to facilitate the central collection of data regarding treatment failure in children and adolescents and outcomes of second- and third-line ART.

No conflict of interest

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Long term effect of PI based ART versus NNRTI based ART on neuropsychological functioning in children

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Background: There is increased use of protease inhibitors (PIs) in African children with HIV but their effect on neuropsychological functioning compared to nonnucleoside reverse transcriptase inhibitors (NNRTIs) is unknown. This study evaluated their long-term effect on neuropsychological functioning in Ugandan children.

Materials & Methods: 132 children (51% male), mean age 7.46 years (range 5 to 10 years) who were randomised to PIs and NNRTIs when aged 6 months to 5 years were followed up five years later and assessed for attention using the Test of Variables of Attention (TOVA), working memory, reasoning, learning, visual processing and general cognition using the Kaufman Assessment Battery for Children, second edition, and motor functioning using the Bruininks-Oseretsky Test of Motor Proficiency, second edition. Analysis of covariance was used to compare age adjusted scores between the two groups controlling for height for age z-score (HAZ) and number of malaria episodes during the two years when they were on the trial treatments.

Results: The groups were comparable in age, level of education, socioeconomic index, gender, weight for age z score though the PI group had a higher HAZ (-0.57 vs -1.15, p = 0.01). The PI group had less impulsivity scores on the TOVA (estimated mean difference -0.48; 95% confidence interval (CI): -0.90 to -0.05; p = 0.03). There were no differences between the groups on general cognition (-0.59, 95% CI: -0.41 to 0.29, p = 0.74 motor skills (-0.05, 95% CI: -0.43 to 0.34, p = 0.81), overall attention (0.10, 95% CI: -0.34 to 0.53, p = 0.66) and on other neuropsychological measures.

Conclusion: This preliminary study shows a difference in impulsivity between children who received PI versus NNRTI based ART but not in other domains. These findings should be treated with caution since the effect of HIV subtype and anemia incidence was not assessed.

No conflict of interest

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12-month response to early LPV-based antiretroviral therapy in West-African children

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Background: Field outcomes of early antiretroviral treatment (EART) initiation in children under 2 years of age as recommended in 2010 remains unknown. We described the 12/15-month virologic response to LPV/r based-ART in Burkina Faso (BF) and Côte d’Ivoire (CI).

Materials & Methods: All HIV-infected children under 2 years of age diagnosed and confirmed by DNA-PCR were enrolled in a 12/15-month therapeutic cohort based on LPV/r in...
Ouagadougou, BF, and Abidjan, CI. CD4 % and viral load (VL, Biocentric) were measured three-monthly. Virological success (VS) at 12/15 months (VL<500 copies/ml) and correlates of VS using a logistic regression were assessed. HIV-1 genotyping was performed in children with VL>1000 copies/ml.

Results: In the context of low early infant diagnosis coverage (16% in Abidjan; 29% in Ouagadougou), 226 HIV-infected children under 2 years of age were screened between 05/2011 and 01/2013. Among them, 162 (72%) children were included and initiated on EART. The median age at diagnosis and ART initiation were 8.6 months [IQR: 4.1 to 16.2] and 13.4 months [IQR: 8.3 to 18.6], respectively. 64% of infants were from Abidjan, 53% were girls, 48% were not exposed to a PMTCT-intervention. Mother was the main caregiver in 82% of cases, 68% had access to tap water at home. At inclusion, median CD4% was 19%, median VL was 6 log copies/ml and 56% of the children were classified 3-4 WHO-stage. At 12/15 months on ART, 13 infants have died (8%), 5 were lost-to-follow-up (3%), and 139 were followed (89%). VS was achieved in 73% of children enrolled and in 82% of children alive. When adjusting for country and sex, a 74% and 93% reduction of VS rate was respectively associated with a lack of access to tap water (aOR: 0.26 [0.10-0.73]) and with a father as the main child caregiver compared to mother (aOR: 0.07 [0.02-0.34]). An increase of CD4 greater than 10% between inclusion and M6 was associated with a higher rate of VS (aOR: 5.63 [1.89-16.75] at 12/15 months. At 12-months, 25 of the 28 eligible children had a genotype, 19 (76%) had ≥1 resistance (64% to 3TC; 28% to EFV, 4% to AZT and LPV/r).

Conclusions: In 2011-2013, challenges still remain for improving EART in HIV-infected children in West Africa. Nevertheless, rate of VS on LPV-based EART is high and comparable to those observed in Europe. Lack of tap water and father as the main child caregiver, correlates of lower VS, are probably markers of a poor adherence. These risk factors could be identified at ART initiation and adherence systematically reinforced.

No conflict of interest

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Better growth is associated with higher neurodevelopmental function in HIV-infected infants and better recovery of developmental function during ART


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Introduction: There are few prospective studies of neurodevelopmental outcomes in HIV-infected infants initiating antiretroviral therapy (ART) in Africa. We used the Malawi Developmental Assessment Tool (MDAT) to determine baseline and post-ART change in neurodevelopmental function in hospitalized children initiating ART.

Materials & Methods: Children were identified from an ongoing trial (NCT02063880) of hospitalized, ART naïve, HIV-infected children. The MDAT was administered at baseline (within 1 month of hospitalization, depending on child's health) and 6-months post-ART. Domain Z-scores were calculated based on data for a Malawian norm population (M. Gladstone and colleagues). Baseline and 6-month Z-scores were compared using paired t-tests. Cofactors for change in Z-scores were evaluated using univariate and multivariate linear regression.

Results: Among 53 children with baseline MDAT data, median age was 1.8 years and median CD4% was 18%. Mean gross motor, fine motor, social, and language z-scores were -1.0, -0.9, -0.6 and -1.0, respectively. At baseline, lower C-reactive protein was associated with higher language skills (p=0.05). Better nutritional status (weight-for-age (WAZ) and height-for-age (HAZ) were associated with higher MDAT scores with p-values ≤0.05 in all...
Abstract

The objective of this study was to describe the prevalence of the G516T genotypes among a cohort of HIV infected women and children in Canada, and associated clinical correlates.

Materials & Methods: HIV infected women and children were recruited from the Centre maternel et infantile sur le SIDA (CMIS) mother-child cohort between 2013-2014; family members were excluded from the study. DNA was extracted from saliva samples, and genotyping was performed using CYP2B6-G516T specific amplification and restriction fragment length polymorphism (PCR-RFLP).

Results: Genotyping was performed on 89 subjects (46 women, 43 children). Self-described ethnic distribution was African (46.1%), Haitian (31.5%), Caucasian (12.4%), and mixed origin (10%). Overall, 38.2% were GG (rapid metabolizers), 49.4% were GT, and 12.4% were TT (slow metabolizers). Among Africans, the GG genotype was most prevalent (46.3%), followed by GT (41.4%) and TT (12.2%). Among Haitians, the GT genotype was most prevalent (64.3%), followed by GG (21.4%) and TT (14.3%). Among Caucasians, 54.5% were GG, 36.4% were GT, and 9.1% were TT. There was a significant difference in the proportion of rapid metabolizers (GG) between Africans and Haitians (46.3% vs 21.4%, p=0.04), with an equal distribution of the GG genotype between patients from West Africa (43%) and Sub-Saharan Africa (44%). The highest proportion of slow metabolizers (TT) was among West Africans (21.5%), while the highest proportion of rapid metabolizers was among European Caucasians (75%). Among children treated with standard (weight/kg) doses of Efavirenz for whom unadjusted drug levels were available, 4/6 (67%) of GG genotype had trough drug levels in the lower therapeutic range (1-2 mg/L) at steady state, as compared to only 3/8 (38%) among the GT genotype. The single child with TT genotype had supra-therapeutic levels (>10mg/L) on standard dosing.

Conclusions: In this study population, the heterozygous GT genotype dominated, though there were significant differences within the predominant ethnic groups represented. Population-based knowledge of these genotypes may help tailor standard NNRTI dosing regimens to optimize their efficacy.

No conflict of interest
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**High Levels of Virological Failure and HIV Drug Resistance in Children on Treatment in Maputo, Mozambique**

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**Background:** Since 2005, access to pediatric ART services has increased in Mozambique, although challenges remain with the first line regimen (AZT/3TC/NVP), assuring quality of care and treatment monitoring. We conducted an evaluation of virological failure (VF) and HIV drug resistance (DR) in children on ART to address these concerns.

**Materials & Methods:** From August 2013 to March 2014, children aged 1-14 years on ART for at least 12 months were consecutively enrolled in six urban health facilities located in Maputo, Mozambique. Clinical and demographic data were collected by using a standardized questionnaire and chart review; Blood was collected for dried blood spots and plasma. Plasma HIV-1 viral load (VL) was measured and those with VF (VL ≥ 1.000 copies/mL) were tested for DR. All statistical analysis accounted for clustering within sites.

**Results:** A total of 713 children with mean age of 103 months (95% confidence interval (CI): 81-125) were enrolled in the study. At enrolment, the median time on ART was 60 months (CI: 39-81); 20% (CI: 15%-27%) had history of PMTCT exposure, 4% (CI: 2%-10%) were severely immunosuppressed and 5% (CI: 3%-9%) had weight/age Z score <-3. From the enrolled children, 73% (CI: 44%-91%) were receiving ART regimen based on d4T/3TC/NVP, 21% (CI: 6%-52%) on AZT/3TC/NVP, 1% (CI: 0%-5%) on a lopinavir-based regimen, 5% (3.1, 10.0) other ART regimens. VF was found in 36% (CI: 27%-46%, n=256) of children, of which 96% (n=245) were genotyped, and 96% (CI: 85%-99%, n=234) of these genotyped revealed ≥ one major DR mutation. These mutations conferred intermediate or high levels of resistance to ≥ one NRTIs in 91% (CI: 88%-94%) [d4T-27%, AZT-27%, 3TC-91%, ABC-32%]; NNRTIs in 94% (CI: 87%-97%) [NVP-94%, EFV-93%]; and PIs in 1% (CI: 0%-4%) [LPV-0.4%]. 90% (CI: 87%-92%) children had intermediate or high levels of resistance to both NRTI and NNRTI classes. Risk factors for DR are current immunosuppression (p=0.0004), weight-for-age Z score (WAZ) < -2 (p=0.04) and decrease of 1 standard deviation (SD) from peak WAZ (p=0.001).

**Conclusions:** The study found relatively high levels of VF and DR in ART-experienced children. DR was associated with current severe immunosuppression and low WAZ. The current pediatric second line regimen (ABC/3TC/LPV/r) was compromised in almost 1/3 of the children with VF. These findings warrant a multi-dimensional approach to quality improvement in treatment and adherence support, and a reconsideration of the current 1st and 2nd line regimens in Mozambique.

No conflict of interest

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**Efficacy and safety of abacavir-containing combination antiretroviral therapy in HIV infected children: a systematic review and meta-analysis**

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**Abstract:** The aim of this systematic review and meta-analysis was to assess the efficacy and safety of abacavir-containing combination antiretroviral therapy (ART) regimens in HIV-infected children. A comprehensive search of the literature was conducted using MEDLINE, EMBASE, and CINAHL databases. The primary outcome was virological suppression (<40 copies/mL) at 48 weeks of follow-up. Secondary outcomes included immune restoration, adverse events, and treatment discontinuation. A total of 19 studies involving 4,682 children were included in the analysis. Overall, 36% (95% CI: 32%-40%) of children achieved virological suppression. Immune restoration was observed in 71% (95% CI: 68%-74%) of children. The most common adverse event was diarrhea (13%, 95% CI: 9%-17%). Treatment discontinuation due to adverse events was reported in 3% (95% CI: 2%-5%) of children. The results of this systematic review and meta-analysis provide evidence for the efficacy and safety of abacavir-containing ART regimens in HIV-infected children.
Background: Abacavir is one of the recommended nucleoside reverse transcriptase inhibitors (NRTIs) for the treatment of HIV infections among children and adolescents. However, there are concerns that the antiviral efficacy of abacavir might be low when compared to other NRTIs especially among children. There are also concerns that abacavir use may lead to serious adverse events such as hypersensitivity reactions and has potential predisposition to developing cardiovascular diseases.

Materials & Methods: We searched four electronic databases, four conference proceedings and two clinical trial registries in August 2014, without language restrictions. Experimental and observational studies with control groups that examined the efficacy and safety of abacavir-containing regimens in comparison with other NRTIs as first-line treatment for HIV-infected children and adolescents aged between one month and eighteen years were eligible. Two authors independently screened search results, extracted data and assessed the risk of bias of included studies using a pre-specified, standardised data extraction form and validated risk of bias tools. We also assessed the quality of evidence per outcome with the Grading of Recommendations Assessment, Development and Evaluation tool.

Results: We included two randomised controlled trials (RCTs) and two analytical cohort studies with a total of 10595 participants. Among the RCTs we detected no difference in virologic suppression after a mean duration of 48 weeks between abacavir- and stavudine-containing regimens (2 trials; n=326: RR 1.28; 95% CI 0.67 to 2.42) with significant heterogeneity (P=0.02; I²=81%). We also found no significant differences between the two groups for adverse events and death. After five years of follow-up, virologic suppression improved with abacavir (1 trial; n=69: RR 1.96; 95%CI 1.11 to 3.44). For cohort studies, we detected that the virologic suppression activity of abacavir was less effective than stavudine in both the lopinavir/ritonavir (1 study, n=2165: RR 0.79; 95% CI 0.67 to 0.92) and efavirenz subgroups (1 study, n=3204: RR 0.79, 95%CI 0.67 to 0.92) respectively. The quality of evidence from RCTs was moderate for virologic suppression but low for death and adverse events, while that of cohort studies was low for all three these outcomes.

Conclusions: Available evidence showed little or no difference between abacavir-containing regimen and other NRTIs regarding efficacy and safety when given to children and adolescents as a first-line antiretroviral therapy for both the early stage and long term treatment. The findings of this study are not suggestive of any major change in the existing treatment policy. There is a need for adequately powered and well planned RCTs of abacavir-containing cART regimens that are reported according to the CONsolidated Standards of Reporting Trials (CONSORT) guidelines. Further research on abacavir-containing cART regimen should also be geared towards defining the subgroup of HIV infected children and adolescents for whom this regimen will be most beneficial with common comparator regimens such as those containing zidovudine, tenofovir and emtricitabine NRTI backbones with follow-up duration of at least 5 years.

No conflict of interest

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Impact of Implementing “Test and Treat” policy on Paediatric ART enrolments and coverage in Uganda

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Material & Methods: The Ministry of Health launched and disseminated these guidelines to all stakeholders though 3 day health facility based trainings and mentoring during the period January to December 2014. To evaluate the impact of this new policy a comparison was made between the number of children initiated between June-December 2013 and those initiated between January-June 2014.

Results: By December 2014, 1340 (84%) of 1600 ART providing health facilities and 17,238 health workers were trained on the new guidelines. There was a 1.4 fold increase in the number of HIV infected children newly initiated on ART from 5540 in June-Dec 2013 to 9145 in Jan-June 2014. The increase was greater among children aged 5-14years and 2-4 years (2.4 and 1.4 fold respectively), however there was no change among the under 2 year old's. Pregnant adolescents constituted 2.5% (229/9145) of children less than 15 years of age enrolled on ART in Jan-June 2014. Paediatric ART coverage has increased from 22% (43,481/193,500) in December 2013 to 27% (51,305/193,500) in June 2014.

Conclusions: Expanding eligibility criteria increases initiation of older children on ART but to enroll those who are at higher risk of disease progression/mortality, more work needs to be done to improve EID and early case detection.

No conflict of interest
to study growth evolution, and define malnutrition (Z-score < -2 Standard Deviations [SD]). A multivariate logistic regression was conducted to determine associated factors to malnutrition at ART initiation. Twelve-month growth evolution on ART and associated factors were studied using a linear mixed model with a random intercept, slope for time, and an unstructured variance-covariance matrix. For WHZ evolution, a quadratic term was added to the model. Variables on socio-demographic, biologic and clinical characteristics at ART initiation were assessed.

**Results:** Between 2012 and 2014, 161 children were enrolled in the initial cohort. Among them, 64% were from Abidjan, 54% were girls. At ART initiation, the median age was 13.6 months [IQR 7.7; 18.4], median CD4% was 19%, 53% were underweight (WAZ<-2 SD), 52% were stunted (HAZ<-2SD), and 36% were wasted (WHZ<-2SD). Overall, malnutrition at ART initiation was more likely for non-breastfed children, those living in Burkina Faso, and for the oldest (12-24 months). Between baseline and 12 months of ART, mean WAZ increased from -2.39 to -1.47 SD, mean HAZ from -2.25 to -1.82 SD, and mean WHZ from -1.61 to -0.74 SD. At 12 months, 25% remained underweight, 43% stunted, and 11% wasted. Adjusted on co-variables, access to electricity at home, and hemoglobin<9 g/dl were associated with a better WAZ evolution, whereas boys and children at WHO clinical stage I-II were associated with a better HAZ evolution, and older age (12-24 months vs < 6 months), children living in CI and those with hemoglobin<9 g/dl had a better WHZ evolution. Moreover, the severity of malnutrition at baseline, whatever the anthropometric indicator used, was associated with a better growth evolution during the first twelve months of ART.

**Conclusions:** A high prevalence of malnutrition at ART initiation was found among West-African children aged less than 2 years: from one third to one half were malnourished. Despite that, growth has improved, even for the most severely malnourished children, but normal values were not reached for all children. A routine and adequate nutritional supplementation on the top of early ART initiation needs to be investigated to go further.

*No conflict of interest*
and trough (C24) drug concentrations and steady-state AUC_{0-24}. The model was also used to simulate exposures and evaluate the dosing guidelines across weights ranging from 5 to 50 kg.

**Results:** In total 2086 sample concentrations in 651 dosing intervals were included in the analysis. The data was best described using a 2-compartment model with absorption through a number of transit compartments. Significant predictors of pharmacokinetics identified by the model were weight (incorporated in the model through allometric scaling) and a composite genotype vector 516GT/983TC on clearance. Patients 516GG/983TT (n=55) were classified as extensive metabolisers (clearance for average child of 15.3kg was 6.65 L/h), heterozygote mutants for one of the SNPs (516GG/983TC – n=56, or 516GT/983TT – n=10) as intermediate (CL=4.75 L/h), individuals 516TT/983TT (n=30) or 516GT/983TC (n=12) as slow (CL=1.76 L/h) and one patient with a rare 516GG/983CC genotype as ultra-slow (CL=0.733 L/h). Basing the classification on SNP 516GT alone, 14.2% of the patients would be miscategorised. As expected, large variability in exposure was encountered between the patients, but the average exposure across weight bands in the CHAPAS-3 study was generally similar, with median C12 ranging between 1.35 and 2.49 mg/L. Model-based simulations using the same proportions of CYP2B6 genotypes in each weight band confirmed that the proposed dosing, achieves comparable exposures across weight bands.

**Conclusions:** These results confirm that the new dosing guidelines tested in the CHAPAS-3 study satisfactorily adjust for the effect of weight. Dosage guidelines based on genotype should take into consideration the combined effect of 516GT and 983TC SNP vector. The groups at particularly high risk of efavirenz overexposure, which may lead to side-effects and possibly affect adherence, are patients heterozygote for both 516GT and 983TC and wild type 516GT patients who are homozygote mutants for 983TC.

**Conflict of interest:** Andrzej Bienczak received funding from EDCTP.

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**CD4 Response in Pediatric Patients on HAART with Sustained Virologic Control**

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**Background:** Previous studies of CD4 response to antiretroviral therapy in adults and children have followed mixed cohorts of adherent and nonadherent children, usually for 1-3 years. The results of those studies have suggested that peak CD4 response occurs within 2-3 years of initiation of therapy and is limited by CD4 nadir and patient age. A PACTG study which followed both adherent and nonadherent pediatric patients on HAART for 5 years showed that patients with initial CD4% <15% did not achieve improvement to above 25%. However, a recent study in adult veterans who were virologically suppressed on HAART showed ongoing CD4 improvement over more than 10 years. This current study evaluated highly adherent pediatric patients with sustained viral suppression on HAART. This abstract reports an expanded cohort from a previous analysis with a smaller patient group.

**Materials & Methods:** Retrospective chart review of HIV + patients from a single clinic in the southwestern United States, ages 0-21 years, on HAART with CD4 counts and viral loads available prior to HAART initiation, as well as at least 2 data points per year. Patients must have maintained viral suppression with only one viral load discrepancy > 1,000 copies allowed for the duration of the study. CD4 response was followed from initial treatment for as long as patients remained suppressed. Means/medians and standard deviations were calculated from time- adjusted CD4, CD4%, CD8,CD8% and CD4/CD8 ratios at 1 year intervals and displayed graphically. SPSS was utilized to conduct repeated measures ANOVA of CD4 Absolute, CD4 Percent and CD4/CD8 ratios over time.
Results: 42 patients remained adherent and virologically suppressed after initiation of HAART, 19 male, 23 female, ages 6 weeks to 16 yrs at diagnosis (mean 4.78 yrs) with 6 acquired, 36 vertical transmissions. Patients were followed at least 2 yrs up to 16 yrs (mean 6.67 yrs). Eight patients (19%) had greater than 12 years of viral suppression. Baseline CD4 counts ranged from 25-4400 (mean 1008), CD4% 2.8-50 (mean 25.88); viral loads 273 to >750,000 (mean 250,135). Plateaus in the CD4 graph began between 2.5 and 5.5 years after the start of HAART. Independent of age and initial CD4 count, CD4 % stabilized and increased throughout 15.5 years of therapy. Repeated measures ANOVA showed CD4 absolute (F(2.502,.031) = 3.383, p=.000), CD4 percent (F(1.841,38.657) = 6.607, p=.004) and CD4/CD8 ratios (F(2.299,39.079) = 11.082, p=.000) differed significantly between pre, 1, 2, and 5 years post initiation of therapy. All 28 patients suppressed > 5 years of therapy achieved > 25% CD4. All 11 patients suppressed > 10 years achieved 32% and 2 patients with data from 16 years were above 41%.

Conclusion: Unlike previous studies, this study suggests that children who remain adherent to HAART can experience ongoing immune healing for as many as 12-16 years. An initial study with a subset of the current cohort was presented at IAPAC 9th International Conference on HIV Prevention and Treatment Adherence, June 8-10, 2014, Miami, FL.

No conflict of interest

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Paediatric antiretroviral coverage among African priority countries

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Background: Adequate provision of antiretroviral medicines is one of the prong targets of the Global Plan towards the elimination of new HIV infections among children by 2015. This is very essential because children are more prone to rapid progress of HIV disease to advanced stage especially when they are not properly managed. The outcomes of various prevention of mother-to-child-transmission programmes in the Global Plan priority countries are very crucial to the goal of virtual elimination of new HIV infections among children and keeping their mothers alive. The objective of this study is to evaluate the progress made and trend in the provision of antiretroviral medicines for children in the 21 priority countries in Africa.

Materials and Methods: A secondary data extraction and analysis were done on the 2014 Joint United Nations Programme on HIV/AIDS (UNAIDS) Global Plan progress report. 2009 and 2013 mid-point estimates of Global Plan Prong 4 Target: Antiretroviral therapy coverage among children aged 0-14 years old was used for this study. Matched-pairs t-test was carried out to evaluate the trend of coverage. Data was analysed using statistical package Stata version 12.0. The p value of <0.05 was considered statistically significant.

Results: The paediatric antiretroviral coverage in 2009 was 10.95% and 23.52% in 2013 among the priority countries, (mean difference 12.57%; 95% confidence interval [CI] 7.64 - 17.50; p=0.0001). In terms of coverage for paediatric antiretrovirals, Botswana led the others with 84% coverage in 2013. Botswana, South African and Swaziland progressed by 41%, 36% and 23% respectively. Cameroon, Chad, Cote d’Ivoire and Congo Democratic Republic made a progress of 3%, 3%, 3% and 0% respectively.

Conclusions: There is a significant progress in the paediatric antiretroviral coverage among the African priority countries. The paediatric antiretroviral coverage is still very low and far lesser to that of the adult HIV-positive individuals on antiretroviral medicines. Southern African countries performed better than their other sub-regional counterparts while the Western African countries progressed marginally. Congo Democratic Republic was stagnated on one spot with no increase in coverage. There is urgent need to boost the coverage across board especially in countries that are poor performers. Efforts must be made to improve access to essential medicines, each
country should prioritise key implementation actions and make efforts to remove numerous bottlenecks at different levels. The countries should request for technical and financial support from international and bilateral partners and must judiciously utilise resources to strengthen healthcare delivery services. The findings of this study will guide healthcare policy makers and practitioners to re-strategise on how to accomplish the elimination of HIV in children and to point out research gaps for future research efforts.

No conflict of interest

Abstract: 38

ARV Treatment of pediatric HIV infection

T-cell activation and treatment outcomes among infants receiving early ART


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Introduction: Chronic immune activation is associated with HIV disease progression in adults; however, data in children, especially infants, are limited. We determined levels and correlates of T-cell activation and the effect of baseline activation on response to antiretroviral treatment (ART) in HIV-infected infants.

Materials & Methods: This investigation utilized specimens from the Optimizing Pediatric HAART study of early infant ART (NCT00428116), in which 99 Kenyan infants less than five months of age were enrolled between 2007-2010 and started on ART.

Peripheral blood mononuclear cell (PBMC) samples collected before ART initiation were analyzed using flow cytometry and the activated (HLA-DR+/CD38high) T-cell percentage quantified. Factors associated with T-cell activation at baseline were identified using Mann-Whitney U tests or linear regression. The effect of baseline activation on survival, CD4 reconstitution and HIV-1 log10 viral load (VL) suppression was assessed using Cox proportional hazard models.

Results: Among 72 infants with available samples, median age at enrollment was 3.7 months, median VL was 6.6 log10 copies/ml and median CD4 was 19%. Most infants had symptomatic disease; 49% were WHO stage 3/4, median weight-for-age Z-score (WAZ) was -2.5 and median length-for-age Z-score (LAZ) was -2.1. Twenty infants died, including 8 before ART initiation. Median CD8+ T-cell activation at baseline pre-ART was 17.0% (interquartile range [IQR] 10.4, 31.8) and median CD4+ T-cell activation was 3.3% (IQR 1.6, 5.8). At enrollment, CD8+ T-cell activation was associated with younger age (-0.15%/day, [95% Confidence Interval (CI) -0.28, -0.01], p=0.05) and weight-for-age Z-score (2.4%/WAZ standard deviation, [95% CI 0.64-4.2], p=0.02), but not with CD4% or VL. CD4+ T-cell activation at enrollment was inversely associated with CD4% (-0.20%/CD4% [95% CI -0.36, -0.05], p=0.01). T-cell activation pre-ART was not associated with time to CD4% reconstitution or VL suppression. Low CD8+ T-cell activation (<5%) was associated with mortality (hazard ratio=3.8 [95% CI 1.3, 11.4], p=0.02).

Conclusions: Contrary to findings in adults, low CD8+ T-cell activation was strongly associated with mortality in this infant cohort. Among infants, low CD8+ T-cell activation in symptomatic HIV infection may be a marker of ineffective immune response.

No conflict of interest
Abstract: 39

**ARV Treatment of pediatric HIV infection**

**Immunologic disruptions in ART naïve HIV+ children and adolescents with preserved CD4 cell counts**

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**Introduction:** Current WHO guidelines recommend initiation of antiretroviral therapy (ART) immediately in all children less than 5 years, and when CD4 cell counts fall below 500 cells/mm³ in older children and adolescents. Evidence supporting these recommendations is largely based on adult studies with limited pediatric data. We inquired whether children and adolescents with CD4 counts above 500 cells/mm³ exhibit immunologic disruptions associated with HIV disease progression. We specifically investigated immune activation, microbial translocation, and CD4:CD8 ratios that correlate with HIV morbidity and mortality.

**Materials & Methods:** We evaluated peripheral blood samples of 75 perinatally-infected HIV+ and 41 unexposed HIV negative (HIV-) children between ages 5-18 years from Bomu Hospital in Mombasa, Kenya collected in 2011-2012. HIV+ children were divided into ART naïve with CD4 >500 cells/mm³ (CD4-high, n=29), ART naïve with CD4 <500 cells/mm³ (CD4-low, n=15), and virally suppressed on ART (ART+, n=41). Cryopreserved peripheral blood mononuclear cells were stained with surface antibodies CD3, CD4, CD8, CD38, CD45RO, and HLA-DR, and intracellular Ki67 then analyzed by flow cytometry. Plasma sCD14, indicating monocyte activation secondary to gut microbial translocation, was measured by ELISA (R&D). Statistical analysis was performed with GraphPad Prism using Mann-Whitney test.

**Results:** CD4-high had CD4 counts and percentages lower than HIV- (count p=0.0107, %CD4 p<0.0001) and ART+ (count p=0.0111; %CD4 p=0.0018). CD4:CD8 ratios were lower in CD4-high compared to HIV- (p<0.0001) and ART+ (p=0.0090). Plasma viral load was similar in CD4-high and CD4-low (medians (IQR) 4.7 (4-5.2) and 4.9 (4.2-5.3) log copies/ml respectively) and higher than ART+ (p<0.0001). There was no significant difference between activated CD38+HLA-DR+ CD8 and CD4 T cells in CD4-high and CD4-low. However, compared to HIV-, CD38+HLA-DR+ CD8 cells were higher in CD4-high (p<0.0001) and CD4-low (p=0.0090). Similarly CD38+HLA-DR+ CD4 T cells were increased in CD4-high (p<0.0001) and CD4-low (p=0.0002) compared to HIV-. Activated CD38+ and Ki67+ memory CD4 T cells were also elevated in CD4-high (CD38 and Ki67 p<0.0001) and CD4-low (CD38 p=0.0143; Ki67 p=0.0001). Finally, CD4-high and ART+ had plasma sCD14 levels higher than HIV- (p=0.0016 and p=0.0067 respectively). Data subanalyses dividing the cohort into children 5-9 years and adolescents 10-18 years yielded similar results.

**Conclusions:** ART naïve HIV+ children and adolescents who maintain CD4 cell counts >500 cells/mm³ nonetheless have persistent HIV viremia, decreased CD4 counts and percentages, and diminished CD4:CD8 ratios compared with HIV- and ART+. More importantly, they have substantial immune activation marked by elevated CD38+HLA-DR+ CD4 and CD8 T cells and increased CD38+ and Ki67+ memory CD4 T cells. Interestingly CD4-high and CD4-low had similar proportions of activated CD4 and CD8 T cells, while ART+ had significantly lower frequencies of these activated cells compared to CD4-high, suggesting ART may partially dampen inflammation. CD4-high also had higher plasma sCD14, providing evidence of gut mucosal disruption and microbial translocation. Thus ART naïve HIV+ children and adolescents exhibit systemic immune activation despite preserved CD4 cell counts. Early ART initiation may protect them from pathologic sequelae associated with persistent inflammation including impaired neurocognitive development, early cardiovascular disease, metabolic complications, and premature death.

*No conflict of interest*
Abstract: 40

ARV Treatment of pediatric HIV infection

Disruption of regulatory T cell subsets correlates with advancing disease in HIV infected children

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Introduction: Regulatory T cells (Tregs) serve as sentinels of the human immune system, mediating self-tolerance and inflammatory responses via suppressive functions. During HIV infection, Tregs may act beneficially to curb immune activation or pathologically to suppress HIV-specific immune responses. Identifying true Tregs with suppressive activity proves challenging during HIV infection, as traditional Treg markers, CD25 and FOXP3, may transiently upregulate expression as a result of immune activation. Helios is an Ikaros family transcription factor that marks natural Tregs with suppressive activity and does not increase upon activation. We evaluated Treg subsets by FOXP3 co-expressed with CD25 or Helios and their association with HIV disease progression in perinatally-infected HIV+ children.

Materials & Methods: We evaluated peripheral blood samples from 93 perinatally-infected HIV+ and 46 unexposed HIV negative (HIV-) children ages 5-20 years from Bomu Hospital in Mombasa, Kenya. HIV+ children comprised 48 ART naïve (ART-) and 45 on ART (ART+). Cryopreserved peripheral blood mononuclear cells were stained for surface antibodies CD3, CD4, CD25, CD38, CD45RO, intracellular Ki67, and transcription factors FOXP3 and Helios, then analyzed by flow cytometry. Plasma sCD14, indicating monocyte activation secondary to gut microbial translocation, was measured by ELISA (R&D). Statistical analysis was performed with GraphPad Prism using Mann-Whitney and Spearman's correlation tests.

Results: Paired comparison of memory CD25+ or Helios+ Tregs in HIV-, ART-, and ART+ all showed higher FOXP3+Helios+ than FOXP3+CD25+ memory Tregs (p<0.0001). Memory FOXP3+Helios+ Tregs were expanded in ART- and ART+ compared to HIV- (p<0.0001). Memory FOXP3+Helios+ Tregs negatively correlated with %CD4 (p=0.0065, r=-0.2547) and CD4:CD8 ratios (p=0.0005, r=-0.3238). In viremic HIV+, plasma HIV RNA levels correlated with memory FOXP3+Helios+ Tregs (p=0.0004, r=0.4499). Plasma sCD14 was elevated in ART- (p=0.0049) and ART+ (p=0.0011) compared to HIV- and correlated with memory FOXP3+Helios+ Tregs (p=0.0407, r=0.1929). HIV+ had higher activated CD38+HLA-DR+ CD4 and CD8 T cell frequencies compared to HIV- (p=0.0001) that correlated with memory FOXP3+Helios+ Tregs (p<0.0001, CD4: r=0.3690, CD8: r=0.3938). HIV+ had increased activation markers CD38 and Ki67 on memory CD4 T cells compared with HIV- (CD38: ART+ p=0.0001, ART+ p=0.0010; Ki67: ART+ p<0.0001, ART+ p=0.0070) that correlated with memory FOXP3+Helios+ Tregs (CD38: p<0.0001, r=0.4117; Ki67 p<0.0001, r=0.4325). CD38 expression on memory FOXP3+Helios+ Tregs was higher in ART- compared to HIV- (p=0.0089) and ART+ (p=0.0311). ART- had elevated memory FOXP3+Helios+Ki67+ Tregs compared to HIV- (p=0.0017). Finally, the percent of CD38+ and Ki67+ cells in memory CD4 T cells and FOXP3+Helios+ Tregs correlated strongly (p<0.0001; CD38: r=0.6380, Ki67: r=0.7258).

Conclusions: Identifying Tregs by FOXP3 co-expression with Helios rather than CD25 revealed markedly higher Treg frequencies, particularly in HIV+ children. Regardless of ART, HIV+ children had a selective expansion of memory FOXP3+Helios+ Tregs. The rise in memory FOXP3+Helios+ Tregs correlated with declining HIV clinical status, indicated by falling CD4 percentages and CD4:CD8 ratios and increasing HIV plasma viremia and systemic immune activation. Finally, memory Tregs expressed immune activation markers CD38 and Ki67 mirroring levels in memory CD4 T cells. Overall, HIV infected children had significant disruptions of memory Tregs that were associated with advancing HIV disease.

No conflict of interest
Abstract: 41

ARV Treatment of pediatric HIV infection

Atazanavir pharmacokinetics–pharmacodynamics in HIV-1-infected children aged 3 months to <11 years treated with atazanavir powder/ritonavir liquid: PRINCE-1 & 2 studies

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Background: Establishing correct dosing for antiretroviral (ARV) therapies in HIV-1-infected children presents challenges owing to increased drug clearance and limited pharmacokinetic data compared with adults. PRINCE-1 (NCT01099579) and PRINCE-2 (NCT01335698) are clinical trials assessing the safety, efficacy and pharmacokinetics of once-daily atazanavir powder formulation boosted with ritonavir liquid (ATV/r), at weight-based doses targeted to provide ATV exposures (area under the concentration-time curve in one dosing interval, AUCτ) in five ATV/r baseline weight-based dosing categories (5 to <10kg =150/80mg; 5 to <10kg =200/80mg; 10 to <15kg =200/80mg; 15 to <25kg =250/80mg; and 25 to < 35kg =300/100mg) with those from earlier adult studies (n=33). Repeated ATV C_{trough} measurements (24h post-dose) available up to Week 48 explored relationships between ATV composite C_{trough} (within-subject geometric mean of all values) expressed as quartiles (CCQ) with virologic efficacy (n=124; observed values) and key safety parameters (n=143).

Results: Of 146 children included in this combined analysis, 49% were male; 57% Black/African American; and 62.3% were ARV-experienced. AUCτ geometric means (% coefficient of variation) at steady state were 32503 (61), 39519 (54), 50305 (67), 55687 (45), and 44329 (63) ng·h/mL in the five ATV/r dosing categories, respectively; and in adults receiving ATV capsules 300mg + ritonavir 100mg were 44185 (51) ng·h/mL. Proportions with HIV-1 RNA <50 copies/mL at Week 48 were 13/32 (40.6%), 24/32 (75.0%), 19/32 (59.4%), and 13/28 (46.4%) in the lowest through highest ATV CCQs, respectively. Mean changes from baseline in total bilirubin at Week 48 were +0.3, +0.5, +0.6, and +1.0 mg/dL in the lowest through highest ATV CCQs, respectively. Corresponding changes for total amylase were +7.8, -10.2, 0, and -17.1 U/L. The proportions with adverse events (AEs) of diarrhea by Week 48 were 4/36 (11.1%), 9/36 (25.0%), 9/36 (25.0%), and 8/35 (22.9%) in the lowest through highest ATV CCQs, respectively. Corresponding proportions with AEs of hyperbilirubinemia by Week 48 were 1/36 (2.8%), 4/36 (11.1%), 5/36 (13.9%) and 13/35 (37.1%), respectively.

Conclusions: ATV exposures were similar in infants and children receiving weight-based dosing of ATV/r compared with exposures in adults, although lowest in infants weighing 5 to <10kg receiving ATV/r 150/80mg. Virologic suppression showed no apparent trend with ATV CCQs, being optimally associated with the 2nd and 3rd ATV CCQs. Consistent with ATV inhibition of uridine-5’-diphospho-glucuronosyltransferase-1A1, total bilirubin levels and AEs of hyperbilirubinemia increased across ATV CCQs. Other laboratory values or AEs did not vary systematically across ATV CCQs. Thus, weight-based dosing of ATV/r plus optimized dual NRTIs achieves virologic suppression in young HIV-1-infected children similar to that with other ARVs, and with a safety profile comparable to that in adults receiving ATV/r.

Conflict of interest: Employee of Bristol-Myers Squibb
ARV Treatment of pediatric HIV infection

Safety and efficacy of atazanavir powder and ritonavir liquid in HIV-1-infected infants and children aged from 3 months to <11 years: the PRINCE-2 study

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Background: Antiretroviral (ARV) treatment options are limited for infants and young children, for whom high viral replication and limited availability of palatable formulations present challenges. A wider range of ARV therapies is therefore needed.

Materials & Methods: PRINCE-2 (NCT01335698) is an ongoing prospective, international, multicenter, single-arm, clinical trial assessing the safety, efficacy and palatability of a once-daily oral powder formulation of atazanavir boosted with ritonavir liquid (ATV/r) plus optimized dual NRTI background therapy in ARV-naïve and -experienced children with screening HIV-1 RNA ≥1000 copies/mL. Children aged 3 months to <11 years and weighing ≥5kg and <35kg were dosed according to five ATV/r categories based on baseline weight bands: 5 to <10kg =150/80mg; 5 to <10kg =200/80mg; 10 to 15kg =200/80mg; 15 to <25kg =250/80mg; and 25 to <35kg =300/100mg. Cumulative efficacy and palatability until Week 24 and safety until Week 48 are presented.

Results: Of 99 treated children: 83 (83.8%) and 56 (56.6%) completed at least 24 and 48 weeks of study therapy, respectively; 64.6% were from Africa; with 62.6% ARV-experienced and age range between 3-120 months. At baseline, proportions with HIV-1 RNA >100,000 copies/mL were 52.2%, 83.3%, 61.9%, 40.0% and 25.0% in the five ATV/r dosing categories, respectively. No deaths or unexpected safety events were reported. Over 48 weeks: the most common adverse events (AEs) were upper respiratory tract infections (33.3%), gastroenteritis (28.3%), vomiting (21.2%), and hyperbilirubinemia-related (18.2%; none in the 5 to <10kg weight band and none leading to treatment discontinuation); serious AEs in 20.2%; and Grade 3-4 elevations of amylase occurred in 33.7% (90.1% had normal pancreatic amylase) and of total bilirubin in 9.2%. AEs led to discontinuation in 7 children (acute pancreatitis/increased amylase / hyperlipasemia (n=1) [5 to < 10kg band receiving ATV/r 150/80mg]; pulmonary tuberculosis (n=1) and abnormal amylase (n=1) [5 to <10kg band receiving ATV/r 200/80mg]; raised ALT/AST (n=1) and vomiting (n=1) [10 to <15kg band]; tuberculosis (n=1) [15 to <25kg band]; and increased amylase / vomiting / abnormal product taste (n=1) [25 to <35kg band]). A child in the 15 to <25kg weight band had an AE of atrioventricular block (mild intensity, duration 11 days, not requiring intervention, ATV/r continued uninterrupted). At Week 24: proportions with virologic suppression (HIV-1 RNA level <50 copies/mL) varied across the five ATV/r dosing categories and were 10/23 (43.5%), 2/12 (16.5%), 10/21 (47.6%), 19/35 (54.3%), and 5/8 (62.5%), respectively, but without differing meaningfully between ARV-naïve and -experienced patients. However, virologic efficacy was lowest in the 5 to <10kg =ATV/r 150/80mg group, likely due to high baseline viral load and a 66.7% discontinuation rate (lack of efficacy [n=1], AE [n=2], withdrawal of consent [n=2], lost to follow-up [n=1], poor compliance [n=1], other [n=1]). At Week 24, 87% and 81% of caregivers reported no trouble giving ATV powder and RTV liquid, respectively.

Conclusions: The palatability of ATV powder, virologic suppression efficacy and the lack of unexpected safety findings compared with previous pediatric and adult ATV studies, suggests that atazanavir powder formulation is a potential new treatment option for HIV-infected children aged ≥3 months to <11 years.
Implementation research on PMTCT and pediatric treatment programs

Antiretroviral Therapy (ART) rollout to health centres in Malawi, Uganda and Zimbabwe: What about the children?


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Background: Lablite is working with Ministries of Health to evaluate rollout of ART in non-research sites in Malawi, Zimbabwe and Uganda. Each comprises a district hospital with surrounding rural primary care (PC) facilities. PMTCT Option B+ started at all facilities during the project. Across Africa, ART coverage in children lags behind adults.

Materials & Methods: Routine individual patient data on 7,260 adults and 718 children have been collected and analysed so far from ART registers during local decentralisation of general ART services from 07/2011-12/2013 in Malawi (5 facilities), 10/2012-08/2014 in Uganda (3 facilities) and 09/2013-08/2014 in Zimbabwe (4 facilities). Updated analyses will include data on additional 2,674 adults and 306 children (total ~1,000 children) from 15 facilities (including an additional district hospital and 2 surrounding health centres in Northern Uganda), and updated to February 2015.

Results: In the district hospitals, children <15 years constituted 207(14%), 60(9%), and 34(9%) of ART initiations in Malawi, Zimbabwe and central Uganda respectively. In PC, corresponding numbers were 368(8%), 37(8%) and 12(6%). In Malawi at the hospital and 2 PC facilities (with general ART before Option B+) there was a modest transient increase in numbers of children initiated on ART in the year following B+ implementation (from 47 to 54 per quarter pre- and post-B+ respectively). In Zimbabwe at the hospital and 2 PC facilities there was an immediate increase from 18 to 40 in the first quarter post-B+ but in the second quarter initiations fell to 17. Median(IQR) age at initiation was 3(1-7) years in Malawi (33%≤2 years) and 3(1-6) years in Uganda (39%≤2 years); ages were similar in secondary and PC (difference p=.53, p=.90 respectively). In Zimbabwe, median(IQR) age at initiation at the hospital was 3(2-6) years (37%≤2 years) but older at 9(3-12) years in PC (14%≤2 years; p<.001).

Pre-ART CD4s were mostly below thresholds for initiation in children >5 years where recorded (median(IQR) CD4 Zimbabwe 297 (180-380) (n=28/41), Uganda 346 (262-477) (n=18/46), not provided in Malawi). In Zimbabwe, 20/24 children >10 years started TDF-based regimens. Children 3-10 years mostly started AZT- (18/34), or d4T-based regimens (7/34), but TDF-based regimens (using adult formulations) were used in 26% (9/34) children. Most (19/24, 25/34 respectively) took NVP. 33/39 children ≤3 years started NVP-based regimens (21/8/4 with AZT/d4T/TDF respectively). only 6 infants (all NVP-exposed) started LPV/r and this was undertaken at the district hospital. In Uganda, most children started AZT/3TC/NVP (38/46), although 6/18 ≤24 months started D4T/3TC/NVP. Regimens are not recorded on the Malawi ART registers.

Conclusions: HIV-infected children are being treated successfully with NNRTI-based ART in rural primary care facilities. Lopinavir/ritonavir is so far only being used for younger children at one Zimbabwean hospital; updated data will provide more information on this. A significant minority of children are receiving tenofovir, although only available as part of an adult unscored tablet, thus likely to have dosing...
inaccuracies. As ART roll-out continues, training must provide healthworkers with knowledge to test and treat children, particularly outside PMTCT programmes; paediatric formulations need to be available everywhere through National programmes.

No conflict of interest

Abstract: 44

ARV Treatment of pediatric HIV infection

Duration and outcomes of the first-line antiretroviral therapy in a cohort of pediatric HIV-infected patients in Yekaterinburg, Russia.

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Background: Russian Federation follows national pediatric ART guidelines largely based on WHO recommendations. Data on the pediatric ART and outcomes in HIV-infected children in Russia are limited. The objective of this study was to evaluate the composition and duration of the first line ART regimen in children with HIV infection in Russian Sverdlovsk Ural region in Yekaterinburg.

Materials & Methods: This was retrospective analysis of the cohort of pediatric HIV-infected patients receiving care at the AIDS center in Yekaterinburg, Russia. The study conducted review of the clinical database and collected data on the composition and duration of the first line ART in HIV-infected children. Collected variables included age of the HIV diagnosis, antiretroviral drugs (ARVs) combinations and duration of first-line ART. Clinical parameters included CD4 counts and HIV resistance and RNA viral load. Descriptive statistics were used for the analysis.

Results: Among 268 registered pediatric HIV patients in care, 200 children (92 boys, 108 girls) with median age 8.3 years (range: 0.4 -14.7 years) were on ART at the time of the study. Median age of starting ART was 2.9 years (0.1-12 yrs). Large majority of the first line ART represented 2 NRTIs+PI (69%; n=138) and 2 NRTIs+NNRTI (27.5%; n=55). LPV/RTV was a preferred PI (83%) and NVP was a preferred NNRTI (93%). Among NRTIs 3TC was the most frequently used ARV, followed by RTI phosphazide, ABC, ddI, and less frequently AZT and d4T. Approximately half (52.5%; n=105) of children remained on the first line ART with undetectable viral load with longest duration of first-line ART of 9.6 years. Twenty children (10%) switched first line ART with undetectable HIV RNA because of changes in ARV formulary. Twenty seven children (13.5%) had detectable viral load with confirmed resistance after median duration of ART of 0.9 yrs (range: 0.3-8.9 yrs). These children were switched to second-line ART in median 1.4 years (0.3-3.9 yrs) after detectable viremia. The median CD4 count and CD% at the time of switch to second line in children with viral resistance were 1168 cells/mm$^3$ (500-2500 cells/mm$^3$) and 30.8% (19-48%), respectively. The majority of children with viral resistance were on NVP based first line ART (59.3%; n=16). Other reasons for switching the first line included ARV associated toxicity (7.5%; n=15), self-discontinuation based or refusal of ART (8%; n=16) and switch to more optimal ART by the provider (1.5%). Most common toxicities included hepatotoxicity and lipodystrophy primarily associated with LPV/RTV based ART.

Conclusions: In our cohort of HIV-infected Russian children more half had sustained virologic suppression on first-line ART. Less than 15 % had developed ARV resistance requiring switch to second-line ART. Other significant reason for switching first-line ART included change in formulary of ARVs, discontinuation by caregiver and ARV-associated toxicity.

No conflict of interest
Abstract: 45

Comprehensive Pediatric HIV care

Factors Associated with Depression among Adolescents Living with HIV in Malawi: A Strong Association with Bullying Victimization

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Background: There is a high estimated prevalence of depression amongst HIV-infected youth with data suggesting a detrimental impact on treatment outcomes. Associated risk factors and correlates of depression amongst HIV-infected youth in sub-Saharan Africa have been poorly examined. This study aimed to identify contributory/protective factors associated with depression in Malawian adolescents living with HIV.

Materials & Methods: This was a cross-sectional study assessing factors associated with depression amongst a convenience sample of Malawian adolescents 12-18 years old living with HIV. Depression was measured by a Chichewa version of the Beck's Depression Inventory version II (BDI-II) and the Children's Depression Rating Scale - Revised (CDRS-R). Data on >70 variables were collected including: socio-demographics, past traumatic events/stressors, behavioural factors, social support and bio-clinical parameters. Chi-square test or two sample t-test was used to explore associations between factors and depression. A second round of screening utilized linear/logistic regression, adjusting for age and sex and identified 18 candidate variables (p< 0.1). Final regression models included variables with significant main effects and interactions.

Results: Of the 562 participants enrolled, 56.1% were females. The mean age was 14.5 years (SD 2.0). Prevalence of depression as measured by the CDRS-R was 18.9% (106/562). In multivariate linear regression the variables significantly associated with higher BDI-II score were female gender, fewer years of schooling, death in the family/household, failing a school term/class, not disclosed or not having shared one's HIV status with someone else, lower level of immunosuppression, and being bullied for taking medications. Bullying victimization was reported by 11.6% of respondents. We found significant interactions: older participants with lower height-for-age z-scores and dissatisfied with their physical appearance had higher BDI-II scores. In multivariate logistic regression: older age OR 1.23 [95% CI 1.07-1.42], fewer years of schooling OR 3.30 [95% CI 1.54-7.05], and being bullied for taking medications OR 4.20 [95% CI 2.29-7.69], were significantly associated with depression.

Conclusions: Fewer years of schooling and being bullied for taking medications were most clearly associated with depression. Programs to support the mental health needs of HIV-infected adolescents that address issues such as disclosure, educational support, and most notably bullying may improve treatment outcomes.

No conflict of interest
Abstract: 46

Comprehensive Pediatric HIV care

Physical activity levels in a cohort of HIV-infected and HIV-uninfected school-aged children in Johannesburg, South Africa

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Background: Despite potential importance to long-term health outcomes adversely affected by HIV, including bone and cardiometabolic health, physical activity (PA) among people living with HIV has not been well studied. We describe PA in South African HIV-infected and uninfected children.

Materials & Methods: Data were obtained from CHANGES (Childhood HAART Alterations in Normal Growth, Genes, and aGing Evaluation Study), a study of perinatally HIV-infected children and uninfected controls in Johannesburg, South Africa from 2012-2014. Age of antiretroviral initiation, HIV-RNA, CD4%, weight-for-age (WAZ) and height-for-age (HAZ) Z-scores, and frequency and duration of physical activities and sedentary behaviors by validated questionnaire were obtained. Metabolic equivalents (METS) of each PA were determined. Moderate-vigorous PA (MVPA) was defined as PA ≥3 METS, while vigorous PA (VPA) was defined as >6 METS. Measures were compared between HIV-infected and uninfected children using chi-squared, t-tests, and linear regression.

Results: 213 HIV-infected and 152 uninfected children aged 6-9 years (83% of target sample) were included. Age, WAZ and HAZ were significantly lower for HIV-infected children.

93.1% of HIV-infected children were virally suppressed (HIV-RNA <400 copies/mL), had a mean CD4% of 37.4, and were initiated on antiretrovirals at a mean age of 8.9 months (SD 6.7). The most commonly reported activities included walking, running, playing, skipping, and active chores. HIV-infected children spent significantly less time in MVPA and VPA than controls (mean difference of 5.1 and 3.3 hours/week, p=0.005 and 0.001, respectively), including less running and skipping. The proportion of children in both groups meeting WHO recommendations for PA was similar. While HIV-infected children reported significantly less total sedentary time than uninfected children overall, the time spent in the various sedentary behaviors did not differ. The most commonly reported sedentary behaviors included watching television, playing computer or phone games, reading, and riding in a vehicle. Differences in VPA, running, and skipping remained significant after adjusting for age; MVPA differences however were no longer significant (adjusted 3.6 hours/week, p=0.052). When adjusted for age, WAZ, and HAZ, only VPA and running remained significant.

Conclusion: Although HIV-infected children initiated early on antiretrovirals with good virologic suppression have high levels of PA, VPA was significantly lower than healthy controls. Further investigation of reasons for these differences in PA and implications on short and long-term health outcomes throughout life are warranted.

No conflict of interest

Abstract: 47

Comprehensive Pediatric HIV care

The creation of a culturally adapted, tablet-based, animated tool for HIV education and post-disclosure counseling of HIV-infected pediatric patients in western Kenya

93.1% of HIV-infected children were virally suppressed (HIV-RNA <400 copies/mL), had a mean CD4% of 37.4, and were initiated on antiretrovirals at a mean age of 8.9 months (SD 6.7). The most commonly reported activities included walking, running, playing, skipping, and active chores. HIV-infected children spent significantly less time in MVPA and VPA than controls (mean difference of 5.1 and 3.3 hours/week, p=0.005 and 0.001, respectively), including less running and skipping. The proportion of children in both groups meeting WHO recommendations for PA was similar. While HIV-infected children reported significantly less total sedentary time than uninfected children overall, the time spent in the various sedentary behaviors did not differ. The most commonly reported sedentary behaviors included watching television, playing computer or phone games, reading, and riding in a vehicle. Differences in VPA, running, and skipping remained significant after adjusting for age; MVPA differences however were no longer significant (adjusted 3.6 hours/week, p=0.052). When adjusted for age, WAZ, and HAZ, only VPA and running remained significant.

Conclusion: Although HIV-infected children initiated early on antiretrovirals with good virologic suppression have high levels of PA, VPA was significantly lower than healthy controls. Further investigation of reasons for these differences in PA and implications on short and long-term health outcomes throughout life are warranted.

No conflict of interest
Background: As vertically HIV-infected children transition into adulthood, determining the best practices to provide counseling for medication adherence and disclosure of HIV status is key to supporting their long-term health outcomes. The AMPATH program provides HIV-related care to 15,000 Kenyan children at over 60 clinical sites, but there are few culturally appropriate tools for children living in East Africa to aid in pediatric HIV care and education. We sought to create a culturally adapted, animated HIV educational tool to be played on Google Nexus 7 Android tablets within post-disclosure counseling sessions with HIV-infected pediatric patients to explain the immunologic and physiologic complexities of HIV at an elementary level.

Materials & Methods: Based on prior qualitative inquiry and consultation with multiple pediatric care providers in western Kenya, we developed potential explanatory metaphors for the animated tool. Storyboards with illustrations created in Adobe Illustrator CS6 were used to outline potential metaphors using appropriate images. We conducted focus group discussions (FGDs) in Kiswahili with adolescents ages 12-18 years, using a semi-structured interview guide to collect qualitative feedback on the acceptability and effectiveness of both the educational content and the imagery of the animation as represented by the storyboards. FGD recordings were translated into English, transcribed, and analyzed by two independent reviewers. These results were used iteratively to revise the storyboards to increase clarity, develop more appropriate imagery, and increase appeal to children and adolescents regardless of tribal identity. Once the storyboards were completed, a native Kiswahili voice actor was recorded narrating in both English and Kiswahili. Narration was imported into Adobe Flash CS6 and synced to animation with the revised imagery of the storyboards. Animations were imported into Adobe Premier and a sound track added. Finished animations in both English and Kiswahili were optimized for Google Nexus 7 Android tablets available in the AMPATH clinical system. Cognitive interviews were then conducted to assess the face validity of the final iteration.

Results: Twenty-four adolescents aged 12-18 (mean age: 15) participated in 4 FGDs to develop the storyboards and educational content. The developmental process yielded an animated HIV educational tool optimized for use on Google Nexus 7 tablets, culturally adapted for Kenya and available in English and Kiswahili. In cognitive interviews with four Kenyan pediatric HIV disclosure counselors working in western Kenya, all concluded the final iteration of the animated HIV educational tool could be an effective resource within HIV disclosure counseling and that the tablet would be simple to integrate into sessions. Counselors also suggested the tool could be used with a wider audience, including caregivers of HIV-infected children and adults living with HIV. One thought watching the animation with the child could enhance the provider-patient relationship. Implementation and evaluation of the impact of the tablet-based tools is now ongoing.

Conclusion: An iterative and culturally adapted approach can be used to create educational materials important to caring for HIV-infected pediatric populations. Furthermore, educational materials that are animated and formatted for use on tablet-based technology are acceptable for counselors in this setting.

Abstract: 48

Comprehensive Pediatric HIV care

‘HIV is like a tsotsi. ARVs are your guns’: Associations between HIV-disclosure and adherence to antiretroviral treatment among adolescents in South Africa

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Introduction: World Health Organisation guidelines recommend disclosure to HIV-positive children by school age to support ART-adherence. However, empirical research on associations between HIV disclosure and ART-adherence among adolescents in Southern Africa is limited. This research examines associations between knowledge of HIV-positive status and ART-adherence among HIV-positive adolescents (10 – 19 years) in South Africa. It was conducted as part of the Mzantsi Wakho study, the largest known mixed-methods study on ART-adherence among adolescents using community-tracing sampling. Findings from the longitudinal panel survey frame the qualitative findings presented here.

Materials & Methods: The study integrated quantitative and qualitative methods in design and implementation. Participants for the qualitative study (n=70) were purposively recruited from the quantitative sample (n=684) to explore disclosure, adherence and defaulting practices in greater depth. Adolescents were defined as being ‘disclosed to’ if they had been informed that they were HIV-positive (‘diagnostic disclosure’), and if they had a basic understanding of HIV and ART. ART adherence was measured by adolescent self-report linked, where possible, to patient markers. In a low-resource health district, all adolescents who had ever initiated ART in a stratified sample of 39 health facilities were identified and traced into 150 communities (n=1102, 351 excluded, 27 deceased, 40 (5.5%) refusals). Interviews used standardized questionnaires linked with clinical records, and statistical analysis was conducted using SPSS 22. Qualitative analysis was premised on 18 months of in-depth interviews and focus groups. Participatory research was complemented by over 700 hours of direct observations with adolescents, caregivers and healthcare workers in clinics, recreational spaces and participants’ homes.

Results: 70% of adolescents knew their HIV status, while 36% reported past-week ART non-adherence. Knowledge of HIV-positive status was associated with higher adherence, independently of all co-factors (OR 2.18 CI 1.47-3.24). Among perinatally-infected adolescents who knew their status, disclosure prior to age 12 was associated with higher adherence (OR 2.65 CI 1.34-5.22). Findings identified strong associations between positive experiences of HIV disclosure and ART-adherence. In clinical settings, disclosure provided an opportunity for adolescents to improve treatment literacy and to access other forms of support. However, disclosure to older adolescents, in particular those who did not know that their long-term medication was for HIV, promoted mistrust and anger towards healthcare workers and caregivers, and was associated with ART defaulting.

Conclusion: Disclosure is an incremental process, with health providers and caregivers providing information about HIV-status in response to a range of clinical and psychosocial demands. Early, comprehensive disclosure is strongly associated with improved ART-adherence among adolescents in this study. However, disclosure of HIV status, to older adolescents in particular, must be conducted cautiously to facilitate good health outcomes, particularly if deception about HIV treatment has been used previously to protect adolescents from stigma and other psychosocial harms.

No conflict of interest
Abstract

Background: A high prevalence of autism spectrum disorder (ASD) was recently noticed among HIV-exposed uninfected (HEU) children followed by a Canadian pediatric HIV program. A review of 296 HEU children enrolled in the Children & Women AntiRetrovirals & Markers of Aging (CARMA) cohort identified 16 children (5.4%) with a confirmed diagnosis of ASD, and a further 3 with strong suspicion of ASD currently being assessed. In total, the number of identified and suspected cases among HEU children represents >4-fold increase over the estimated global prevalence circa 2010 (1.47%). In contrast, only two ASD cases were identified among 141 perinatally infected HIV+ children (1.42%) enrolled in the CARMA cohort. Previous studies have suggested associations between ASD and mitochondrial dysfunction, as well as with maternal infections in pregnancy. Mitochondrial abnormalities have also been observed in children whose HIV+ mothers received antiretroviral treatment during pregnancy. It is well established that HIV and antiretroviral drugs can negatively affect mitochondrial DNA (mtDNA) quantity and quality, in addition to increasing oxidative stress. We investigated blood mtDNA content in HEU children with a diagnosis of ASD (HEU/ASD+) compared to HEU children without ASD (HEU/ASD-) and HIV-uninfected unexposed (HUU) children.

Materials & Methods: Sixteen (n=16) HEU/ASD+ children, 69% male, 75% Black, 25% White, and ranging in age from 2 to 16 years were age, sex, and ethnicity-matched 1:2 with CARMA HEU/ASD- children (n=32). All HEU children were exposed to perinatal antiretroviral therapy. A third group included age and sex-matched anonymous control HUU children (n=32) for whom only sex and date of birth was available. The assumption was made that these children are HIV- and ASD-. Leukocyte mtDNA content was measured via qPCR. Cross-sectional comparisons between the 3 groups were done using unpaired t-test, as data were normally distributed.

Results: Both HEU/ASD+ (n=16, mean ± SD: 56.8± 21.3) and HEU/ASD- children (n=32, 64.9 ± 21.8) had significantly higher leukocyte mtDNA content compared to HUU children (n=32, 45.4 ± 15.8), p=0.043 and p<0.0001, respectively. There was no significant difference between HEU/ASD+ and HEU/ASD- (p=0.23). There were no obvious patterns or differences between the two HEU groups with respect to perinatal antiretroviral exposure (duration or type) although the study was not powered to investigate this.

Conclusions: Our results suggest that children born to HIV+ mothers and exposed to perinatal antiretroviral therapy have higher blood mtDNA levels. This finding is consistent with previous studies in younger HEU children, which suggested this increase to be a compensatory mechanism in response to mitochondrial dysfunction. While HEU/ASD+ and HEU/ASD-children had similarly increased blood mtDNA content compared to HUU, it remains to be seen whether distinct qualitative mtDNA changes leading to increased content may differentially predispose to development of ASD. Further work is underway to characterize this cohort of HEU/ASD+ children.

No conflict of interest

Abstract: 50

HIV infection and adolescents

Self-reported HIV Risk Assessment and Risk Factors among Adolescents from the High HIV Prevalence Area in the USA

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Background: Adolescents are at risk for acquiring HIV due to high rates of unprotected sex and sexually transmitted infections (STIs). Youth frequently lack awareness about the risk of acquiring HIV. In Washington, DC, with 2.5% overall HIV prevalence, 0.2% of adolescents (13-19 years) and 1.0% of youth (20-29 years) are infected with HIV. This study aimed to evaluate self-reported HIV risk assessment and risk factors among adolescents tested for HIV at the pediatric Emergency Department (ED) located in a community hospital in Washington, DC.

Methods: A self-reported questionnaire with multiple choice answers on HIV risk and risk factors was offered to adolescents (≥13 years) at the United Medical Center ED during March 2013-August 2014. The questionnaire was distributed after adolescents received their HIV test results. Adolescents with positive HIV test results were excluded from participating in the survey. Descriptive statistics were used for data analysis.

Results: A total of 405 adolescents (median age–16 years) completed the survey. The majority (70%; n=285) were female and Black (95%; n=385). The majority (52%; n=212) reported being sexually active either currently, in the past, or both. Among adolescents with sexual history, more than half (65%; n=137) reported using condoms 'always' or 'almost always'. Half (50%; n=105) reported that they knew their partner's HIV status. Almost a third (29%; n=61) of sexually active youth reported at least one prior STI, with 80% reporting chlamydia (n=49) and 30% gonorrhea (n=18), with 15% (n=9) reporting both STIs. The large majority of surveyed adolescents (91%; n=369) did not believe that they were at risk for acquiring HIV.

Conclusion: In an urban area with a high HIV prevalence, majority of tested and surveyed predominantly female adolescents did not believe that they were at risk for acquiring HIV. Although more than half of adolescents with sexual history reported using condoms consistently, almost a third of them had a history of at least one STI. Better understanding of young people’s perception of their risks for HIV and STIs is important in order to develop effective messaging and communication with youth about risks and prevention of HIV and STIs.

No conflict of interest

Abstract: 51

HIV infection and adolescents

Growing up with perinatal HIV: a life not expected.

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Introduction: Centers for Disease Control and Prevention (CDC) estimate that nationwide there are close to 10,000 survivors of the perinatal HIV infection (PHIV) who are living in the United States. The unique experience by the PHIV-infected young adults present an opportunity to describe qualitatively what it is like to grow up with PHIV in the United States. The purpose of this phenomenological study was to interpret the perceived journeys, lived experiences, learning experiences, and situations that affected youth who grew up with PHIV.

Materials & Methods: The study enrolled PHIV-infected young adults (>18 years of age) receiving care at the perinatal HIV program in metropolitan DC area. The primary form of data collection was the individual face-to-face 60 minute interview with open-ended questions. The interviews were recorded and transcribed verbatim. The lived experience was classified using Van Manen’s four lifeworld existentials,
Results: Seventeen PHIV infected patients aged 18-24 years participated in the study. The overarching themes expressed by participants were living a ‘life that was not expected’ and living a ‘harsh life’ while growing up with HIV. Most of the young adults reported lived space as surrounded by ambiguity, hoping never to have to disclose their HIV status. Hospitalizations or clinic appointments were reported as places where they experienced less stressful emotions because their HIV status was known. The participants had very few expectations for their own lives and lacked anticipation for others to help them improve their lives. A great majority of the young adults described emotional experiences of anger, fear, stigma and loneliness while growing up with HIV. Most of the young adults with PHIV had vivid memories of being told of their HIV status. The anger was described as experience around the time their HIV status was disclosed to them. Fear of others finding out was related to a felt need to protect self and the emotional burden to protect the mothers and other members of the family. The mother figure was central in the young adult’s life and most of the orphaned participants revealed a life void of a parent after the mother died. Among those whose mothers were alive, the young adults still longed for an alternate confidant with whom to discuss their HIV status. Only 4 (24%) of the participants revealed they had close family and friends’ involvement in their lives. The youth with PHIV also reported missing out on reaching their goals for education and employment.

Conclusion: Our results suggest that better understanding of the lived space, lived body, lived time, and lived relation is needed to develop services and intervention that provide in depth understanding and support to the adolescents and young adults who have grown up with PHIV.

No conflict of interest

Abstract: 52

HIV infection and adolescents

“I want to be called daddy”: needs assessment of sexual and reproductive health among perinatally infected adolescents in Zambia

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Background: Expanded access to antiretroviral therapy has improved survival of perinatally infected children in sub-Saharan Africa. They are reaching the age of adolescence and facing new challenges on sexual and reproductive health (SRH). This study examined challenges and needs of SRH among HIV-positive adolescents.

Materials & Methods: A cross sectional study was conducted at the University Teaching Hospital of Zambia from April to July 2014. In total, 200 HIV-positive adolescents who were aged 15 to 19 years, and already aware of their HIV-positive status were recruited. They administered structured questionnaires including open-ended questions. Descriptive analysis was done about their basic background, knowledge of HIV transmission, self-disclosure of HIV status, SRH-related issues and behavior. Concerns about marriage and intention to have children were manually categorized into emerging themes. For the participants aged less than 17 years, we obtained written consent from their caregivers.

Results: A total of 190 adolescents were included in the analysis: 110 girls (57.9%); and 80 boys (42.1%). At the time of the survey, only three were not attending school. They had correct knowledge about reducing the risk of HIV transmission by having sexual intercourse with one uninfected partner (59.8%) and by condom use (78.4%), the risk of mother-to-child transmission of HIV (91.0%), and availability of drugs that can prevent HIV transmission to
children (81.5%). At the time of survey, 33.2% were in intimate relationship, while 20.0% had ever disclosed their HIV status to their partners, then 13.2% were rejected by the partners, and 73.7% obtained supportive relationship. Regarding current SRH issues, they felt comfortable to talk with friends (16.8%), nobody (16.3%), mothers (15.8%), and HIV-positive peers (9.5%). About 67.9% knew how to tell a person with whom he/she does not want to have sexual intercourse. Pharmacy/clinic/hospital were the major places to obtain condom (47.9%) and birth control methods (56.8%). Regarding future SRH issues, 44.2% had concerns about their marriage. Major concerns emerged from 59 (70.2%) answers were ‘fear of disclosing to partner’ (44.1%), and ‘potential risk of HIV transmission to partner and children’ (30.5%). Meanwhile, majority (80.5%) had intention to have children in the future. Of those who responded the reasons (68.4%), emerged themes were ‘Child is a gift/blessing’ (22.3%), ‘I want to be a father/mother or have my family’ (15.4%), ‘Having a child is normal’ (11.5%), ‘I love children’ (10.0%), and ‘I want my successors’ (9.2%). Regarding sexual experience, 38 (20 %) had ever had sexual intercourse at their median age of 16 years and partners’ median age of 18 years. At the first sexual intercourse, 21 had already known their HIV status, 18 used condom, and 7 had forced sexual intercourse.

Conclusions: HIV-positive adolescents are sexually active, and vulnerable to risky sexual intercourse. They also have unmet needs for the future marriage and family life. Adolescents’ needs for sexual and reproductive health should be comprehensively addressed in HIV care/treatment program.

No conflict of interest

Abstract: 53

HIV infection and adolescents

Lower ANC Attendance and PMTCT Uptake in Adolescent versus Adult Pregnant Women in Kenya

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Background: Although rates of pregnancy and HIV infection are high among Kenyan adolescent women, their engagement in PMTCT services is poorly characterized. We hypothesized that adolescent women show lower engagement in the PMTCT cascade than adult women, from antenatal care (ANC) attendance to HIV testing and antiretroviral (ARV) uptake.

Materials & Methods: We conducted a nationally representative cross-sectional survey of mothers attending 120 maternal child health clinics selected by probability-proportionate-to-size-sampling in Kenya in July-December 2013, with a secondary survey oversampling HIV-positive mothers in 30 clinics. Self-report questionnaires verified by clinic booklets recorded ANC attendance, HIV testing, ARV use and maternal characteristics. Data were compared between adolescent (age <20) and adult mothers. Differences in maternal characteristics were assessed by Chi-square test. Logistic regression was used to analyze ANC attendance and HIV testing among all women and ARV uptake among HIV-positive women.

Results: Among 2521 mothers surveyed, 278 (12.8%) were adolescents. Adolescents were less likely than adults to have above primary education (25.0% vs. 42.9%, p<0.001),
intended pregnancy (40.5% vs. 58.6%, p<0.001), and a current partner (73.1% vs. 90.9%, p<0.001). Overall, 2471 (97.8%) reported attending ≥1 ANC visit. Among 1859 women with verified ANC visits, 898 (44.7%) attended ≥4 visits. Adolescents were less likely than adults to attend ≥4 ANC visits (35.2% vs. 45.6%, OR[95%CI]=0.65[0.49-0.86]). This effect remained significant when adjusting for education, primigravida, pregnancy intention and HIV status (aOR[95%CI]=0.59[0.36-0.97]). Among 2359 women who attended ≥1 ANC visit and were not known to be HIV-positive prior to pregnancy, 2298 (96.1%) received HIV testing during pregnancy. Testing rates were not significantly different between adolescents and adults. Among 288 HIV-positive women who attended ≥1 ANC visit and were not on HAART prior to pregnancy, 20 (6.9%) were adolescents, and 243 (84.4%) used any ARVs for PMTCT. Adolescents were less likely to use ARVs than adults (65.0% vs. 85.8%, OR[95%CI]=0.31[0.12-0.81]).

Conclusions: Adolescent mothers showed poorer ANC attendance and lower uptake of ARVs for PMTCT. This calls for further study on barriers to ANC and PMTCT services among adolescent women and development of targeted interventions to improve uptake and retention of this vulnerable population through the PMTCT cascade.

No conflict of interest

Abstract: 54

HIV infection and adolescents

48-month pregnancy incidence among HIV-infected female adolescents in Côte d'Ivoire, 2009-2013

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Introduction: Previous evidence indicated that HIV-infected adolescents had sexual desires and were engaged in corresponding risky behaviors in industrialized countries, little is known however to inform their fertility, especially in sub-Saharan Africa. We estimated in West Africa the 4-year pregnancy incidence and associated factors among HIV-infected female adolescents in care.

Materials & Methods: We conducted a retrospective analysis of data collected from 2009 to 2013 in Abidjan, Côte d’Ivoire, within the pediatric cohort of the International epidemiological Databases to Evaluate AIDS (ieDEA) West Africa Collaboration. Female HIV-infected adolescents aged 10-19 years, having at least one clinical visit in 2009 were included. Data on new (incident) pregnancies were obtained through medical records and interviews with health professionals. Pregnancy incidence rate was estimated per 100 person-years (PY). Poisson regression models were used to identify factors associated with the first pregnancy and provided incidence rate ratios (IRR) with 95% confidence intervals (CI).

Results: Overall, 266 female adolescents were included in 2009, with a median age of 12.8 years (IQR: 10.0-15.0), CD4 cell counts 506 cells/mm³ (IQR: 302-737) and 80% on antiretroviral treatment. They contributed to 939 PY of follow-up. Over the 48-month follow-up period, 17 new pregnancies were reported: 13 girls had one pregnancy while two had two pregnancies. The incidence rate of pregnancy was 1.8/100 PY (95% CI: 1.1-2.9). The highest incidence was observed among those aged 15-19 years at baseline: 3.6/100 PY (95% CI: 2.2-5.9) (adjusted IRR: 14.2, 95% CI: 1.9-108.2; ref. girls aged < 15 years). Maternal orphans seemed to be at higher risk compared to non-orphans, however the difference was at the limit of statistical significance (adjusted IRR: 14.2, 95% CI: 1.9-108.2; ref. girls aged < 15 years). Maternal orphans seemed to be at higher risk compared to non-orphans, however the difference was at the limit of statistical significance (adjusted IRR: 3.1, 95% CI: 0.9-11.0). There was no association between the baseline levels of hemoglobin and CD4 cell counts with the occurrence of first pregnancy.
Conclusions: The incidence of pregnancy among HIV-infected adolescents in care was high in Côte d'Ivoire. More targeted and age-adapted sexual and reproductive information and services should be provided before 15 years of age. Vulnerability of maternal orphans merits further investigation.

No conflict of interest

Abstract: 55

HIV infection and adolescents

Higher risk of sexually transmitted infections among perinatally HIV-infected female adolescents despite lower behavioral risks reported than HIV-negatives

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Background: Perinatally HIV-infected female adolescents (paHIV) are reported to be at increased risk of sexually transmitted infections (STI) due to limited access to and availability of preventive sexual health services. We assessed the impact of behavioral characteristics on the prevalence of common STIs in a cohort study examining the natural history of human papillomavirus (HPV) infection in paHIV and HIV-negative female controls in Thailand and Vietnam.

Materials & Methods: PaHIV and HIV-negative female adolescents, matched in a 1:1 ratio by age and lifetime number of sexual partners, were enrolled. Baseline behavioral risk characteristics were collected through an audio-computer-assisted self-interview, and STI screening included syphilis serology and testing of cervical samples for Chlamydia trachomatis, Neisseria gonorrhoea, HSV-2, and HPV genotypes (Roche Linear Array test). We used multiple logistic regression to calculate odds ratios (OR) and 95% confidence intervals (CI) for associations between behavioral factors with any high-risk HPV or any STI. Backwards stepwise selection was used, successively dropping the covariate with the highest P-value until all remaining terms were significant at P <0.2.

Results: Baseline data from 92 paHIV and 92 matched HIV-negative controls were assessed. Median (IQR) age was 18 (17-20) years and median lifetime sexual partners was 2 (1-3). None ever received HPV vaccine. More HIV-negative females lived with parents than paHIV (59% vs. 26%, P=0.001). paHIV were less likely to never use condoms in the previous 6 months (11 vs. 41%, P=0.001), to have used alcohol (39% vs. 55%, P=0.03) or tobacco (8% vs. 16%, P=0.05) in the past 3 months, or ever used illicit drugs (8% vs. 20%, P=0.02) than controls. There was no difference in the proportion who had ever had unsafe or unplanned sex after using alcohol or illegal drugs (paHIV 17% vs. control 20%, P=0.7); 34% of paHIV and 47% of controls had ever been pregnant (P=0.14). Among the paHIV, the median CD4 count was 579 (378-792) cells/mm³, and 62% had plasma HIV-RNA <40 copies/mL. Any cervical high-risk HPV was present in 42% of paHIV vs. 30% of controls (P=0.09) and any STI was present in 68% of paHIV and 50% of controls (P=0.01). Chlamydial and gonorrheal infections were detected in 25% and 4% of paHIV vs. 21% and none of controls (P=0.48 and P=0.12, respectively). In multivariate analysis, HIV-infection (OR 3.42, 95%CI 1.62-7.22; P=0.001), ever having unsafe or unplanned sex after using alcohol or illicit drugs (OR 8.58, 95%CI 2.42-30.44; P=0.001) and inconsistent condom use over the past 6 months (OR 4.17, 95%CI 1.71-10.17, P=0.0023) were independently associated with an increased risk of any prevalent STI at baseline. Ever having been pregnant was independently associated with a lower risk of prevalent STI (OR 0.40, 95%CI 0.20-0.90; P=0.01).
**Conclusions:** Being HIV-infected, having sex after using alcohol or illicit drugs, and unsafe sex were the major contributing factors to STIs among female adolescents. Our data support the need for greater integration of preventive sexual health services into HIV care programs for pAHIV females and more effective linkages between existing programs.

**No conflict of interest**

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**Abstract: 56**

**HIV infection and adolescents**

Exploring new entry points to increase identification and enrolment of HIV positive children and adolescents into care, treatment and support in Dar es Salaam, Tanzania

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**Introduction:** Tanzania, like many other countries, faces challenges in identifying HIV positive children and adolescents who need life-saving antiretroviral treatment. PASADA, a faith-based organization that supports 20 health facilities in Dar es Salaam, is implementing various HIV testing and counselling (HTC) strategies, with referrals of HIV positive clients to care, treatment and support, according to national norms and guidelines. Dar es Salaam has an estimated HIV prevalence of 6.9% among adults (8.2% females; 5.3% males), 4.0% among youth (6.3% females; 1.0% males) and shoulders a significant proportion of the national HIV burden (17% and 24% respectively among adults and youth) (Tanzania HIV and Malaria Indicator Survey (2011)).

**Materials & Methods:** A total of 12 HTC strategies, categorised as health facility-based, institution-based and community-based, were implemented from January 2014 to March 2015. For each, PASADA compiled the number of people tested, as well as their age, sex and test results.

A total number of 26,434 individuals were tested (53% females; 47% males). Of the total, 19% were children aged 0-14, 29% aged 15-19, 27% aged 20-24, and 25% aged 25 and above. Across all age categories, HIV positivity rates were higher among females than males. The strategies that identified the highest proportion of HIV positive children aged 0-14 were HTC among faith healers’ patients (HIV positivity of 13.3%; number tested n=15), provider-initiated testing and counselling (PITC) to children with signs of tuberculosis (TB) (11.1%; n=11), facility-based HTC for children of PLHIVs (8.1%; n=247), HTC of children of producers and clients of local brews (6.9%; n=101) and HTC at private dispensaries (6.4%; n=125). Providing HTC in schools (0.5%; n=2015) yielded the lowest proportion HIV positive children aged 0-14.

**Results:** Strategies yielding the highest proportions of HIV positive adolescents aged 15-19 were HTC among traditional healers’ clients (17.4%; n=23), PITC to adolescents with signs of TB (16.7%, n=17), HTC among men who have sex with men (MSM) (12.5%; n=8), facility-based HTC for children of PLHIVs (9.8%, n=22) and HTC of producers of local brews and their clients (7.3%; n=55). For young adults aged 20-24 years, the most effective strategies at high risk targeting PITC to patients with signs of TB (29.7%; n=17), HTC outreach (12.0%; n=25), HTC in schools (9.0%; n=367), HTC among MSM (7.7%; n=26) and HTC among faith healers’ patients (7.1%; n=196). These same strategies were also most effective at identifying HIV positive adults aged 25 and above.

**Conclusions:** A combination of health facility-based and community-based HTC strategies was successful in identifying HIV positive children and adolescents. As an organisation with a good understanding of the sociocultural context and health seeking behaviours of their population, PASADA identified additional entry points for HTC beyond the traditional health facility and outreach approaches. Expanding provision of HTC to clients of faith/traditional healers, at private dispensaries, and offering HTC to individuals of all ages at ‘hotspots’ such
as locations where local alcohol is brewed may offer additional opportunities to increase paediatric and adolescent ART coverage in certain contexts.

No conflict of interest

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HIV infection and adolescents

Age-based Differences in Referrals for Individual Psychosocial Counseling in Adolescents Attending a Pediatric ART Clinic in Lilongwe, Malawi

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Introduction: Adolescents living with HIV (ALHIV) experience multiple psychological and emotional distresses, which can have a great impact on their adherence to anti-retroviral therapy (ART) and their overall physical and mental health. Individual sessions with a trained psychosocial counselor can be beneficial in guiding them towards positive living. There is limited data on reasons for counseling among ALHIV, especially in resource-limited settings. This study aimed to evaluate the reasons for referral to a psychosocial counselor for individual therapy sessions to better understand the specific needs of ALHIV.

Materials & Methods: Retrospective chart review of individual psychosocial counseling referrals from June 2013 to December 2014 was done to identify the most common primary reasons for referral for adolescents attending a pediatric HIV clinic in Lilongwe, Malawi. The number of sessions until completion of therapy was also evaluated. Fischer’s Exact Test was used to evaluate for age (younger teens 11-15 years versus older teens 16-22 years) or gender related differences.

Results: 217 ALHIV aged 11-22 years were referred for individual psychosocial counseling during this time period, accounting for 60% of overall individual counseling referrals for the clinic and 18% of the 1197 active adolescents. 64% (n=138) were females, and 36% (n=79) were males, which does not reflect the gender variance in clinic enrollment for this age group (50.5% females, 49.5% males). 55% (n= 119) were younger teens, and 45% (n= 98) were older teens. 48% of adolescents have completed treatment, requiring an average of 4 sessions for younger teens and 3 sessions for older teens. The remaining 52% are still undergoing active counseling. The most common reasons for referral were depression (12.9%), anger (13.4%) and fear of dying (12.9%). Younger teens had significantly higher prevalence of fear of dying (p= 0.025) and confusion (p= 0.007), and older teens had significantly higher prevalence of body image issues (p= 0.022). There were no differences in reason for referral based on gender

Conclusions: To improve treatment and prevention of psychosocial problems in ALHIV, programs should focus on the most common issues of depression, anger, and fear of dying. Age-based differences were observed in this study, indicating improved programming focusing on fear of dying is needed for younger teens. In general, younger teens require more sessions to complete individual psychosocial therapy, and females were more often referred.

No conflict of interest

Abstract: 58

HIV infection and adolescents

Recruitment Methods for a Pre-Exposure Prophylaxis (PrEP) Study with Adolescent and Young Adult Men Who Have Sex with Men (MSM)

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Introduction: Successful recruitment of youth into biomedical HIV prevention trials is critical for drug licensure and implementation of novel prevention strategies among populations most vulnerable to HIV. Recruitment methods for young adults may differ from those for adolescent minors. We present recruitment strategies and screening data from two Adolescent Medicine Trials Network (ATN) PrEP studies with adolescent (ages 15-17, ATN 113) and young adult (ages 18-22, ATN 110) men who have sex with men (MSM) in the United States.

Methods: Twelve sites participated in ATN 110 and 6 participated in ATN 113. Eligible participants were sexually-active, HIV-negative, biological males who reported recent HIV transmission risk behavior. Multiple recruitment methods were employed across sites, including street and venue-based outreach, community and school presentations, and online advertising on social media websites and social networking apps. Eligibility data was collected through screening tools programmed into iPod Touch and web-based forms and documented on recruitment logs.

Results: Recruitment for ATN 110 ran from March to September, 2013, and for ATN 113 from August 2013 to September 2014. For ATN 110, of the 2186 individuals approached for screening, 921 declined to be screened (42%), 865 were ineligible (40%), 122 were eligible but declined participation (6%), 277 were eligible and scheduled for a study visit (13%), and 200 were enrolled. For ATN 113, of the 1873 individuals approached, 527 declined screening (28%), 1102 were ineligible (59%), 144 were eligible but declined participation (8%), 100 were eligible and scheduled for a study visit (5%), and 79 were enrolled. Adolescents were less likely to decline eligibility screening (p<.01), but more likely to be ineligible than young adults (p<.01). Significantly fewer eligibility screenings were done via in-person venues for ATN 113 (5.3%) than for ATN 110 (40%).

Conclusions: Enrolling an adolescent cohort of MSM into a PrEP trial required more time than the young adult cohort. While adolescents approached were more agreeable to being screened, they were much less likely to be eligible for the study than young adults. Online recruitment strategies were much more successful than in-person strategies at finding eligible adolescent participants. Ultimately, study sites that were able to use a combination of online and in-person approaches were most successful at meeting enrollment goals.

No conflict of interest

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Implementation research on PMTCT and pediatric treatment programs

Early HIV diagnose among HIV exposed infant in central Mozambique

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Introduction: To reduce of mother to child HIV transmission from 28% in 2012 to less 5% by 2015, improvements in pediatric HIV cares and early ART for HIV-positive infants are strategic priorities for the Mozambique Ministry of Health (MOH). Mozambique National Institute of Health founded by National Academy of Science of United States of America is conducting implementation research to address high postpartum (PP) loss-to-follow-up (LTFU) of mothers and HIV-exposed infants in six health facilities in the Sofala and Manica provinces of central Mozambique. The research has ethical national IRB approval and has 4 main question : (1) What is the PCR test waiting time at Health facilities since this is collected until mother reception of results, (2) What is the number of HIV exposed infant with early HIV diagnose (3) what’s the waiting time to start (Highly Active Anti-retroviral therapy (HAART)
Abstract

Since the infant were sample collected; (4) what are main factors related to LTFU.

Methods & Materials: We conducted formative research with patient flow mapping at all 6 HF, 49 key informant interviews, and 12 focus group discussions 6 with patients and 6 health workers and we analyzed health facility data at CRC and . The study had two phases. The first phase (formative) where conducted from September 2014 to January 2015 qualitative for interview, focal group discussion and quantitative methods was used. Data were collected on the waiting time of PCR for the early diagnosis of infants exposed to HIV in 6 US study.

Results: A total of 1237 HIV exposed infants attended at child at risk care (CRC ) 54.8% (n = 679) had a blood sample taken for PCR testing, of these 66% (446) of mothers received the PCR result, 15% (67) had positive result and of these 24% (16) began HAART. The wait time from PCR sample collection to sending of the sample to the laboratory ranged from 1 to 12 days with an average of 5 days. The wait time from sending the sample to the arrival of the results ranged from 14 to 43 days with an average of 28. The wait time from sample collection to initiation of HAART ranged from 35 to 136 days with an average of 86 days. Respondents mentioned the weakness of mother's advice and/or caregivers of HIV exposed infant, lack of man involvement, afraid of her husband for disclosure of HIV status, stigma at the community family level interfere with care through HIV care services.

Conclusions: Despite the efforts undertaken at the HF level to reduce time of HIV diagnosis in HIV exposed infant, there are still many difficulties in this process. The wait time for PCR test results continues to be a big gap hindering early diagnosis of HIV in exposed infant and delaying early initiation of HAART. At the community level stigma is still high to HIV positive people, interfering with initiation and retentions on HIV care services.

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Implementation research on PMTCT and pediatric treatment programs

Impact of Option B+ on maternal ART initiation rates in Mashonaland Central Province, Zimbabwe

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Introduction: Zimbabwe's PMTCT Program began its transition to Option B+ ('test and treat for life') strategy in September 2013. With an HIV prevalence of 15.9% among women in antenatal care (ANC), Option B+ presents an opportunity to improve maternal and child health through improved access to ART, reduced transmission to uninfected male partners and provide protection against vertical HIV transmission in future pregnancies in Zimbabwe. Our objective was to document changes in ART initiation rates among HIV positive women in ANC following transition to Option B+ in Mashonaland Central Province.

Material & Methods: In April 2014, Option B+ was rolled out simultaneously to all 135 health sites in Mashonaland Central Province, serving a population of 273,372 women of childbearing age. Routinely collected data from the national PMTCT program on maternal ART initiation rates was analysed descriptively 6 months prior and 9 months after roll out of Option B+ (Oct 2013-Dec 2014). Chi-square test was used to calculate statistical significance.

Results: The simultaneous, rapid roll out of Option B+ to all sites in Mashonaland Central resulted in significant, 457% increase in the number of HIV positive pregnant women initiated on ART in ANC $\chi^2(1, N = 5300) = 2373.43$, $p< 0.0001$, from 6 months prior to 6 months after implementation of B+. Prior to Option B+ implementation, among 1829 HIV positive pregnant and lactating women, 23.2% (n= 424) were initiated on ART. During the first three months of Option B+ implementation,
maternal ART initiation rates were higher (n=1195) than the number of women newly identified as HIV positive in ANC (n=807). In the last quarter of 2014 (Sept-Dec), among 982 women identified in ANC as HIV positive, 95.5% (n= 938) were initiated on ART (95% CI: 94.0% to 96.7%).

Conclusions: Implementation of Option B+ resulted in dramatic and significant increases in the number of HIV positive pregnant women initiated on ART in Mashonaland Central Province. Introduction of Option B+ saw an initial surge in maternal ART initiation rates as HIV positive women in care but not on ART were initiated under revised guidelines. Following this ‘ART catch-up’ phase, initiation rates stabilised proportionate to number of HIV positive women identified in ANC. With high ART coverage, there is need to enhance retention and adherence of mother-baby pairs across the PMTCT cascade. Specific efforts should be placed on improving postnatal retention and adherence, for improved uptake of early infant diagnosis among HIV-exposed infants and timely ART initiation among infected children.

No conflict of interest

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Implementation research on PMTCT and pediatric treatment programs

A population-based estimate of documented completion of early infant diagnosis in Mashonaland East Province, Zimbabwe


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Introduction: In Zimbabwe, information on health services received by HIV positive pregnant women and their exposed-infants across the PMTCT cascade is documented in multiple, paper-based registers at health sites. Summarizing individual completeness of service uptake can only be achieved by manual review and therefore the proportion of mother-baby pairs who uptake timely EID is not routinely reported. We conducted a population based survey in which individual HIV infected mother-baby pairs were followed through registers to better understand probability and determinants of completing EID.

Material & Methods: We selected 45 of 193 health facilities in Mashonaland East Province, serving a population of 297 172 women of childbearing age using a modified probability proportional to size schema. Outcomes of all HIV positive mothers enrolled in ANC from 26-Apr-12 to 30-May-13 were traced through facility registers to determine documented uptake of EID for their HIV-exposed infant within three months of birth. We estimated the weighted probability of EID completion overall and assessed site-to-site variability. Influence of routinely collected facility and individual factors on documented completion of EID was analyzed using Poisson regression with robust standard errors to estimate risk ratios.

Results: We identified 2646 HIV positive women among a population of 18 065 attending ANC in 44 facilities (14.6%); 35.5% (n=939) had documented uptake of EID within three months (95%CI: 31.1%-39.9%). Average EID completion varied across ANC site volume (p< 0.01), but variability within groupings by site size was large and varied by more than 2-fold. After adjustment, gestational age at presentation (Risk Ratio[RR]: 0.97 per two weeks; 95%CI:0.95-0.99; p< 0.01), later calendar time of ANC presentation (RR: 1.04 per 30 days; 95%CI:1.02-1.06, p< 0.01) and smaller site volume were significantly associated with EID completion.

Conclusions: We observed low documented uptake for timely EID among a population-based sample of HIV positive women in ANC. While facility size had a strong influence on the probability of EID completion, dramatic variability within groupings by size indicate need for additional studies to understand facility characteristics related to size as well as local operational factors unrelated to size for effective service delivery. Future research should seek to trace and document true outcomes among
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Implementation research on PMTCT and pediatric treatment programs

The Action Birth Card: Evaluation of an innovative goal-setting tool to increase demand and uptake of underutilized services along the PMTCT cascade

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Introduction: Reducing morbidity and mortality during pregnancy and preventing vertical transmission of HIV requires demand and uptake of services along the PMTCT cascade. The Action Birth Card (ABC) is an innovative goal-setting tool for use by pregnant women to plan uptake of services across the PMTCT cascade in Zimbabwe. Service uptake goals in the ABC were established based on services in the PMTCT cascade with sub-optimal utilization rates. The ABC prompts women to identify barriers to service uptake, problem solve using existing community resources, record and reflect on their performance. The objective of our evaluation was to assess service utilization rates of women who received the ABC in their most recent pregnancy.

Materials & Methods: In November 2014, a cross-sectional survey of women who received the ABC during their most recent pregnancy in Rushinga District, Mashonaland Central Province was conducted. Service uptake related to each ABC Goal during recent (with ABC) and previous (without ABC) pregnancies was documented using a structured, pre-tested questionnaire. ABC Goals include: Uptake of ANC< 14 weeks gestation; Male partner accompaniment to 1st ANC visit; Both partner HIV test in pregnancy; 4+ ANC visits; Birth Plan Development; Facility Based Delivery; and Prompt postnatal care (<3 days of birth) for mother and infant. Proportion of women who made use of services in pregnancies with and without Action Birth Card were compared by Chi-square analysis. To explore potential influence of temporal bias upon service uptake between pregnancies, utilization during the recent pregnancy was compared with national data over a similar period.

Results: Among 174 women interviewed, average age was 26.9yrs (range 16-40yrs) and average number of pregnancies 2.5. Women demonstrated significantly higher service uptake during their recent pregnancy using the ABC planning tool compared to previous pregnancy without ABC for all ABC utilization indicators (p< 0.005), with the exception of 4+ ANC (p=0.07). Dramatic increases in service were seen for early ANC uptake (63% ABC; 36% no ABC); partner HIV status known (94% ABC; 72% no ABC) and prompt postnatal care for mothers and infants (99% ABC; 38% no ABC). Women who used ABCs during their recent pregnancy also demonstrated higher uptake rates than national figures over the same time period.

Conclusions: Rural women who received the Action Birth Card and planned for service use in their recent pregnancy demonstrated higher reported uptake of services along the PMTCT cascade compared to both previous pregnancies and national data. Implementation of this low-cost, effective intervention should be expanded to enhance existing efforts by the Ministry of Health and Child Care to increase demand and uptake for services along the PMTCT Cascade. Service goals in the ABC should be extended to postnatal services in the PMTCT cascade, including early infant diagnosis for HIV-exposed infants and adherence and retention for HIV-infected mothers and infants. Further research should
Abstract

Seek to establish the impact of goal-setting and planning using the ABC upon health and development outcomes of mother-baby pairs.

No conflict of interest

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Implementation research on PMTCT and pediatric treatment programs

Importance of programmatic longitudinal surveillance for identification of congenital anomalies among infants exposed to HIV-1 and antiretrovirals

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Results: Of 2,935 HIV-infected women enrolled in the Mpepu study who delivered live-born infants, newborn exams were documented on 2,900 (99%) infants. ART from conception was documented for 1088 (38%) women; 1147 (40%) started ARVs during pregnancy; 442 (15%) women received AZT monotherapy; and 223 (7%) received no ARVs during pregnancy. A total of 28 congenital anomalies were identified, and 8 (29%) were first diagnosed at a visit after the initial birth exam (Table 1). No differences were identified in the number of infants with or without congenital abnormalities by ARV exposure group in pregnancy, but the study was underpowered to detect differences in rare outcomes. Identification of congenital anomalies after the birth exam occurred either because the anomaly was not readily apparent at birth (e.g. biliary atresia), or because an externally-identifiable anomaly was overlooked at birth but subsequent parental concern led to documentation and management of the anomaly.

Conclusions: ARV use in pregnancy warrants ongoing surveillance monitoring for teratogenicity, particularly for regimens such as EFV/FTC/TDF with insufficient safety data in pregnancy. Nearly one third of birth anomalies detected in this cohort of well children were diagnosed after the initial birth exam. Our findings highlight the importance of incorporating, where possible, longitudinal assessment and reporting for detection of congenital anomalies that may not be identifiable at the birth exam.

No conflict of interest

Background: A large and increasing number of HIV-infected women are conceiving while taking antiretrovirals (ARVs) globally. In resource-limited settings, surveillance systems, if present, often are limited to the initial birth exam.

Materials & Methods: We used pre-randomization data from May 2011-Dec 2014 from an ongoing clinical trial of infant cotrimoxazole prophylaxis in Botswana. Enrollments of live-born infants of HIV-infected women occurred after delivery, so long as the mother consented to infant participation and no infant life-threatening conditions were identified at birth. Infants were examined by study staff at delivery, and monthly in the first 3 months of life, and congenital anomalies were documented. We present a descriptive analysis of anomalies identified after the initial birth exam.
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Implementation research on PMTCT and pediatric treatment programs

Postpartum transfer of care among HIV-infected women who initiated antiretroviral therapy during pregnancy: a cohort study

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Background: The movement in prevention of mother-to-child transmission (PMTCT) programmes to integrate antiretroviral therapy (ART) provision into antenatal care has created the need to transfer women to general ART clinics after delivery for ongoing care. While there are widespread concerns around ART adherence and loss to follow-up after delivery, there are few data describing this postpartum step in the HIV care cascade for women starting ART in pregnancy.

Materials & Methods: We examined postpartum transfer between ART services in a cohort of virally suppressed women who had started ART in pregnancy and were transferred from an integrated antenatal ART clinic to general ART clinics from May 2012 - September 2013. Before transfer, women completed a brief questionnaire and post-transfer engagement in care at an ART clinic was assessed via routine laboratory records and telephonic follow-up.

Results: During the study period 279 postpartum women were transferred to ART clinics (median age, 28 years; median duration of ART use at transfer, 30 weeks). Overall, between 74% and 91% of women had evidence of attending an ART clinic after delivery, depending on the outcome definition. The median time from transfer to reported engagement in ART care and first laboratory assessment was 8 weeks and 22 weeks respectively. In a logistic regression model adjusted for age, CD4 cell count and being diagnosed with HIV in the current pregnancy, additional weeks on ART prior to transfer improved the odds of engagement in care at an ART clinic after transfer (OR 1.04 95% CI 1.00-1.07, p=0.033).

Conclusion: Postpartum transfer of ART care is an important step in the HIV care cascade for PMTCT programmes but one that has received little attention. Even in this cohort, women who were adherent at the time of transfer, up to 26% of women had no evidence of engaging in care at an ART clinic post-transfer, suggesting this is a vulnerable step in the HIV care cascade. To ensure the benefits of ART for both maternal health and PMTCT, retention is required across all steps of the cascade, including transfer of ART care after delivery.

No conflict of interest

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Implementation research on PMTCT and pediatric treatment programs

The performance of virological testing for Early Infant Diagnosis of HIV: A Systematic Review

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Background: Scale up of more effective PMTCT interventions requires review of the existing testing algorithm to optimize infant testing in the context of wider exposure to ARVs as a result of maternal ART and infant prophylaxis. Knowledge of the performance of virological assays at different time points and in the context of ARV exposure is critical to inform such revision. This systematic review had the objective to inform the revision of the World Health Organization (WHO) infant testing algorithm by assessing diagnostic accuracy for virological
testing at birth and at 6 weeks in the context of ARV exposure.

Materials & Methods: The search strategy used, aimed to consider studies published from 2009 (date of the most recent WHO guidelines on infant testing) and included the following search terms: HIV, HIV-1, HIV-2, AIDS, NAAT/NAT, PCR, whole blood, plasma, DBS, newborns, infants, children. PubMed, Embase, Cochrane Library, and Lilacs as well as conference proceedings from CROI, ICASA, IAS, and the International Workshop on HIV Pediatrics were consulted. Studies were included if investigating performance of virological assays, against a standard comparator, in infants exposed to HIV and exposed to maternal ARVs or post-natal prophylaxis. Two independent reviewers conducted the screening and a third reviewer was consulted to resolve discordance. Retrieval of missing information was sought by contacting authors. Summary estimate for performance were calculated. In order to assess the risk of bias the QUADAS-2 tool was used and the overall assessment of the quality of evidence was performed by using the GRADE approach.

Results: A total of 2203 records were screened with final selection of 9 manuscripts. Three studies were included to assess the accuracy of PCR on DBS specimens and in the context of ARV exposure. The pooled sensitivity and specificity were 100% and 99.03% [98.19, 99.88] respectively. The risk of bias was judge as low yet the quality of the evidence, by using the GRADE approach, was considered low due to poor generalizability and low sample sizes. Two studies were identified to assess PCR performance at birth compared to the at 6 weeks of age. The calculated pooled sensitivity and specificity were 67.82% [60.89, 74.76] and 99.73% [99.43, 100] respectively. The risk of bias in these studies was judged low but the GRADE quality of evidence for sensitivity was estimated to be low due to poor generalizability and small sample sizes.

Conclusions: Our systematic review shows that there is currently no evidence to suggest that virological assays on DBS have poor performance when infants are exposed to ARVs. However only few subjects in the studies were exposed to triple maternal ART and postnatal prophylaxis. The performance of PCR at birth demonstrated low sensitivity and high specificity. However, this may reflect the inability of detecting intrapartum infections rather than a lack of accuracy of the assays used. Sensitivity of PCR at birth may therefore vary depending on the transmission dynamics that are influenced by the PMTCT intervention provided. Further research to assess accuracy of PCR at different time-points and in the context of more effective PMTCT interventions is urgently needed.

No conflict of interest

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Implementation research on PMTCT and pediatric treatment programs

Targeted HIV testing for older children of HIV-infected adults increases testing rates & reveals high prevalence of previously undiagnosed infection


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Background: Health systems offer infant HIV testing as part of prevention of mother-to-child HIV transmission (PMTCT) programs, but are not built to systematically diagnose HIV infection in older children before symptomatic illness. Offering HIV-infected adults attending HIV treatment programs targeted testing in home or clinic may increase early diagnosis of children with HIV.
Materials & Methods: HIV-infected parents attending HIV care clinic at Kenyatta National Hospital (KNH) in Nairobi, Kenya were asked about their children’s HIV status. Adults with untested children ≤12 years old chose to test children either at home (HBT) or in a clinic (CBT). Multinomial relative risk regression was used to identify cofactors of testing acceptance.

Results: During the 9-month period at KNH when routinely offering targeted testing was implemented, approximately 4 times as many children were tested per month as in the previous 10-month period (13.6 vs 3.5 per month, RR: 3.9, 95%CI: 2.8-5.5).

Among 116 enrolled adults, 23 (20%) chose HBT and had 46 children tested, 48 (41%) chose CBT and had 58 children tested, and 45 (39%) did not complete testing. More adults chose CBT than HBT (p=0.003), but more children were tested per adult by HBT (2.0 vs 1.2, p<0.001). HIV prevalence among 104 tested children was 8% overall; 6 infected children were identified by CBT and 2 by HBT (median age: 8 years (IQR: 2-11)).

Compared to adults who chose CBT, adults who chose HBT were more likely to have higher income, more education, be male, have a partner, have an unemployed partner, and have a partner known to be HIV negative (p<0.05), while adults who did not test their children were more likely to have higher income and have a partner who was known to be HIV negative or of unknown HIV status (p<0.05). In multivariate analyses, income and partner status remained significantly associated with testing choice.

Conclusions: Targeting HIV-infected parents in care increased the rate of pediatric testing substantially with high prevalence of pediatric HIV. CBT was preferred over HBT at this urban referral hospital. Efforts to increase pediatric HIV testing and to understand parental characteristics are important to provide timely diagnosis and linkage to care.

No conflict of interest

Abstract: 67

Coinfections in Hiv infected children

Tuberculosis co-infection among children on ART in Nigeria

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Introduction: Tuberculosis is common in countries that have high burden of children living with HIV, yet data on Tuberculosis co-infection among children on ART remains limited. The objective was to examine the magnitude of TB co-infection among children on ART and compare their ART outcomes with non-TB counterparts.

Materials & Methods: A retrospective analysis of medical records of children aged <15 years newly initiated on ART between 2011 and 2012 from purposively selected 20 facilities in five states. Structured tools were used to abstract data. STATA software was used to perform descriptive, survival and multivariate analyses.

Results: A total of 1,142 children with the median age of 3.5 years were followed for 24 months. Of these, 95.8% were assessed for TB at ART initiation and 14.7% had TB. Children on ART were likely to be diagnosed with TB if they were 5 years of age or above (p<0.01) and delayed ART initiation (p<0.05). The Cotrimoxazole and Isoniazid prophylaxes were provided to 87.9% and 0.8% of children respectively. The rate of new TB cases was 3 (2.2-4.0) per 100 person-years at 6 month which declined to 0.2 (0.06-1.4) per 100 person-years at 24 months.

The retention among children co-infected with TB at 12 and 24 months was lower than that in the non-infected group (71.9% and 60.2% versus 86.2% and 76.4%). Mortality at 12 and 24 months was higher in TB co-infected children (11.3% and 14.6%) compared to 2.6% and 4.4% respectively. The proportions of LTFU 12 and 24 months were 16.9% and 25.2% for TB co-infected and 11.3% and 19.2% for non-TB infected. The rates of LFTU and deaths at 24 months among TB co-infected were 12.8

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(95%CI: 8.8-18.6) and 8 (5.1-12.8) compared to 8.7(7.3-10.6) and 2.3(1.6-3.2) per 100 person-years respectively. TB co-infection (aHR: 4.3; 2.3-7.9), malnutrition (aHR: 5.1; 2.6-9.8) and those less than 1 year at ART initiation (aHR: 4.0; 1.4-12.0) were associated with death. Similarly, TB co-infection (aHR: 1.3; 1.1-1.6) and children less than 1 year of age at ART initiation (aHR: 2.9; 1.7-5.2) were more likely to be lost to follow up.

**Conclusion:** Children on ART co-infected with TB are less likely to survive and have higher risk to be lost to follow-up. Provision of isoniazid prophylaxis remains low. These findings underscore the urgent need for inclusion of TB/HIV co-infection among children in global plans and reporting mechanisms.

**No conflict of interest**

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**Abstract: 68**

**Coinfections in Hiv infected children**

**Seroprotection after two doses of Neisseria meningitidis C conjugated vaccine and long-term immunity among HIV vertically infected children, in Rio de Janeiro.**

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**Background:** In Brazil, since 2007 all HIV infected children have been immunized with one dose of *Neisseria meningitidis* C conjugated vaccine (C Polysaccharide/CRM197) (MCC) intramuscularly, free of charge. The aim of this study is to describe the long-term immune response (LTR) to MCC, and response after re-immunization (RR).

**Materials & Methods:** HIV-infected patients, aged 2-18 years old, with CD4+ cell > 15% or 350 cell/mm3, without opportunistic disease, without antibiotic use, were enrolled. Protective antibody titer was defined as a serum bactericidal antibody ≥ 1:4 (with human complement). Patients were evaluated at: 1-2 months after (short term response), 12-18 months for LTR and re-immunization, 1-2 months after the re-immunization to evaluate RR. Bivariate analysis was performed. Variables with p-value<0.15 were independently evaluated through logistic regression.

**Results:** 145 children were enrolled; 144 were followed up until LTR evaluation and 135 after RR evaluation. Mean age was 10.9 years, 78 (54%) were female, 79 (55%) had a history of at least one C clinical category (CDC) event during their lives, and 125 (87%) were using HAART. The nadir mean CD4 cells % was 13.5. 57/144 (40%) had post-immunization protective antibody titer after 1-2 months of immunization, 34/144 (23.6%) had LTR, and 108/134 (81%) had RR. Factors associated with LTR were: post-immunization protective antibody titer after 1-2 months of immunization (OR=17.0, 95%CI=5.8-49.6), and higher nadir CD4 cells percent (OR=0.94, 95%CI=0.8-1.0). Factors associated with LTR were: post-immunization protective antibody titer after 1-2 months of immunization (OR=17.0, 95%CI=5.8-49.6), and higher nadir CD4 cells percent (OR=0.94, 95%CI=0.8-1.0). Factors associated with LTR were: post-immunization protective antibody titer after 1-2 months of immunization (OR=17.0, 95%CI=5.8-49.6), and higher nadir CD4 cells percent (OR=0.94, 95%CI=0.8-1.0). Factors associated with LTR were: post-immunization protective antibody titer after 1-2 months of immunization (OR=17.0, 95%CI=5.8-49.6), and higher nadir CD4 cells percent (OR=17.0, 95%CI=5.8-49.6). Factors associated with LTR were: post-immunization protective antibody titer after 1-2 months of immunization (OR=17.0, 95%CI=5.8-49.6), and higher nadir CD4 cells percent (OR=17.0, 95%CI=5.8-49.6). Factors associated with LTR were: post-immunization protective antibody titer after 1-2 months of immunization (OR=17.0, 95%CI=5.8-49.6), and higher nadir CD4 cells percent (OR=17.0, 95%CI=5.8-49.6).

**Conclusions:** The proportion of children with post-immunization protective antibody titer was higher after the second dose of MenC. In order to maximize the immune response, individuals must be immunized when VL is undetectable and CD4 cells are within normal limits even at the re-immunization.

**No conflict of interest**
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Coinfections in HIV infected children

Impact of simplified algorithm for diagnosis of Tuberculosis among children with TB exposure in Mozambique

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Background: In 2014 a new clinical algorithm for the diagnosis and treatment of Mycobacterium tuberculosis (TB) in children was introduced in Mozambique to simplify the diagnosis of TB and increase the number of children receiving treatment. The algorithm specifies that children <14 years of age with TB exposure and signs/symptoms of TB should initiate TB treatment without additional diagnostics, and asymptomatic children <5 years with TB exposure receive isoniazid (INH) prophylaxis. Healthcare workers were trained on the algorithm in April-June 2014. We evaluated the impact of the new algorithm on the identification of TB cases among children <5 years of age with exposure to TB in Nampula province.

Methods: Routinely collected aggregate data were reviewed from 35 ICAP-supported health facilities (HF) that provide TB and HIV services. The number of children <5 years of age identified with exposure to TB, the proportion of TB-exposed children who were screened for TB signs/symptoms and the proportion of children who started INH prophylaxis or TB treatment were compared between 2 periods: pre (October 2013- March 2014) and post (July-December 2014) the new algorithm by means of weighted paired t-tests.

Results: In the ‘pre’ period there were 2,758 TB cases diagnosed and 523 children <5 years were identified as contacts of these TB cases; in the ‘post’ period there were 2,889 TB cases diagnosed and 873 children contacts identified. Among children with TB exposure, 95.6% (501/523) ‘pre’ and 100% (873/873) ‘post’ were screened for TB signs/symptoms (p=0.28). There was no difference in the proportion of children initiated on INH prophylaxis in the ‘pre’ and ‘post’ periods [94.3% vs 93.1%, p=0.80] nor was there a difference in the proportion of children started on TB treatment [1.5% vs 3.8%, p=0.21]. The proportion of children that started either INH prophylaxis or TB treatment among the number of TB-exposed children did not change ‘pre’ and ‘post’ roll out (95.8% vs 96.9%, p=0.78).

Conclusion: In Nampula province preliminary data show that the introduction of the new algorithm, which should lead to easier identification of children with TB and a higher number of children treated for TB, did not result in more children with TB exposure actually being diagnosed with TB. This finding supports the need for increased awareness among healthcare workers to find TB exposed children and for further development of other strategies and tools to improve case detection and treatment.

No conflict of interest

Abstract: 70

Coinfections in HIV infected children

HIV-malaria co-infection in a cohort of Ugandan children hospitalized for acute febrile illness

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Introduction: Dual infection with HIV and malaria fuels the spread of both diseases in sub-Saharan Africa. Implications for diagnosis and management among children hospitalized with fever in areas where both pathogens co-circulate deserve further study.

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Methods: Prospective cohort study. Children (2mo-5yr) hospitalized with acute febrile illness at the Jinja Regional Referral Hospital, Uganda, were enrolled between 15 February, 2012 and 11 April, 2013.

Results: Of 2002 children, 1049 (52%) had a diagnosis of *P. falciparum* (highly specific parasitologic criteria: rapid test positive for both HRP2 and pLDH antigen, and positive thick blood smear). Although universal screening is recommended, HIV testing was performed on only 911/2002 (46%) of the cohort, because of frequent stockouts of the diagnostic test. Among patients who underwent HIV testing, 47/911 (5.2%) were seropositive. HIV-malaria co-infection was found in 12 patients; one patient was older than 18 months. The rate of co-infection was lower than expected, even under the null hypothesis that infections are independent: malaria prevalence 12/47 (26%) among patients with HIV vs 437/864 (51%) among patients without HIV, RR 0.50 (95%CI 0.31-0.83), p<0.001; HIV seropositivity 12/449 (2.7%) among patients with malaria vs 21/198 (11%) among patients without malaria, RR 0.25 (95%CI 0.13-0.50), p<0.001. Among co-infected patients, 5 had severe malarial anemia, 6 impaired consciousness, and 5 respiratory distress; frequencies were not significantly different from HIV seronegative patients with malaria (p>0.05 for all comparisons). None of the co-infected patients died, compared to 3/437 deaths among HIV seronegative patients with malaria (p=1.0). However, HIV seropositivity was associated with higher mortality among patients with non-malarial febrile illness (3/21 (14%) vs 2/177 (1.1%), RR 13 (95%CI 2.2-71), p=0.009).

Conclusions: We observed: (1) high diagnostic yield of HIV testing, supporting Ugandan guidelines for universal screening at hospital admission; (2) need for improved stock management to ensure HIV testing is available; (3) lower rates of malaria-HIV co-infection than expected, perhaps explained by relatively increased susceptibility to pathogens other than malaria among HIV seropositive children; and (4) in contrast to previous studies, no association of HIV co-infection with increased disease severity in and mortality from malaria.

No conflict of interest

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Coinfections in Hiv infected children

High pre-ART viremia and wasting are associated with pneumonia in early treated HIV-infected Kenyan infants

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Introduction: Acute respiratory infections (ARIs) are a major contributor to global child morbidity and mortality. HIV-infected children are particularly susceptible to ARIs. We determined incidence and cofactors of ARIs in longitudinally assessed HIV-infected infants receiving antiretroviral therapy (ART).

Materials & Methods: HIV-infected infants initiated ART at ≤12 months of age and were followed monthly for 2 years in Nairobi. Infants were enrolled from 2007 to 2009 and thus had not received the pneumococcal conjugate vaccine. ARI rates and cofactors were determined using Andersen-Gill Cox regression models for recurrent events. Type of fuel used in the home was used as a proxy for exposure to home air pollution.

Results: Among 111 HIV-infected infants, the median age at ART initiation was 4.5 months. Pre-ART median CD4% was 19% and HIV-1 RNA was 6.6 log10 copies/ml. Almost one-third of infants (29%) were wasted (weight-for-height Z-score (WHZ) <−2). During 24 months on ART (median follow-up time, 22.1 months), upper respiratory infection (URI) and pneumonia incidence was 122.6 and 35.4 per 100 person-years (py), respectively. Thirty-six (35%) infants had at least one episode of pneumonia, and 11 (11%) had 2-4 episodes. Infants with higher pre-ART viral load (HIV RNA >7 log10 copies/ml) had 3.79-fold higher risk of ARI (95% confidence interval (CI), 2.05, 7.01; P<0.001) and infants with wasting had 2.42-fold higher...
risk of pneumonia (95% CI 1.37, 4.26; P=0.002). Infants with both high pre-ART VL and wasting had higher incidence of pneumonia (179.7, 95% CI, 106.4, 303.4 per 100 py) than infants with only one of these risk factors (44.4 per 100 py) or neither (17.0 per 100 py). Among 46 children with household fuel data, URI rates were significantly higher among children with exposure to wood fuel (HR=1.74, 95% CI, 1.17, 2.50; P=0.006).

Conclusions: In early treated HIV-infected infants, higher systemic virus levels and wasting prior to ART were independent risk factors for pneumonia, and infants with wood exposure had higher URI. Further data on influence of air pollution on respiratory outcomes in HIV-infected children will be useful to inform interventions to optimize lung health in this group at high risk for pulmonary disease.

No conflict of interest

Abstract: 72

Coinfections in Hiv infected children

Severe morbidity in HIV-infected children before and after initiating a lopinavir-based therapy before the age of two in West-Africa, 2011-2014

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Background: To describe the incidence of severe morbidity before and after 12 months of early antiretroviral therapy (EART) initiation in West-African HIV-infected children treated before the age of two years.

Materials & Methods: All HIV-1 infected children (confirmed by DNA PCR), <2 years old, whose parents agreed to participate in the MONOD ANRS-12206 project in Abidjan (Côte d’Ivoire) and Ouagadougou (Burkina Faso), were included in an initial therapeutic cohort to receive an EART based on Lopinavir/r twice daily together with a cotrimoxazole prophylaxis and therapeutic education. We documented all severe morbid events (SME), leading to death or hospitalization, during the pre-inclusion period and within the first 12 months on EART. All SME were validated by a pediatric committee. Incidence rates (IR) of SME per 100 child-months (CM) of follow-up were computed with their 95% confidence intervals (CI); there were based on log-transformed IRs to ensure that no interval bound would be below 0 or above 100. We further described the diagnosis spectrum of SME.

Results: From August 2011 to February 2013, 177 HIV-infected children were pre-included (Abidjan: 110; Ouagadougou: 67). Among these, 161 were initiated on EART (Abidjan: 103; Ouagadougou: 58). Before EART initiation, 47 SME occurred in 43 children, overall 9 (21%) died. The overall incidence of SME pre-ART was 35.33 per 100 CM (95%CI: 26.70-47.29). In Abidjan and Ouagadougou, this was respectively 21.37 (95%CI: 13.63-33.50) and 64.62 (95%CI: 44.62-93.59). Before EART, the main diagnoses (n=74) were gastroenteritis (24%), sepsis (16%), severe malnutrition (15%), respiratory infections (12%), anemia (9%), malaria (8%), tuberculosis (7%), others (9%). At EART initiation, median age was 13.5 months; 56% of the children reached WHO stage 3/4, median CD4% was 19% (IQR: 13-26). During the first 12 months on EART, 71 SME occurred in 53 children; 14 (8.6%) children died during the first 12 months of EART. The overall incidence of SME was 3.92 per 100 CM (95%CI: 3.11 – 4.95); it was 2.71 (95%CI: 1.91-3.83) and 6.22 (95%CI: 4.54-8.51) in Abidjan and...
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Ouagadougou, respectively. The main diagnoses (n=97) were gastroenteritis (27%), respiratory infections (24%), malaria (13%), anemia (10%), severe malnutrition (8%), sepsis (7%), others (11%). The median delay to SME after EART was 1.9 months (IQR: 0.7-6.9).

Conclusions: Despite a late access to EART, the incidence of SME was seven times lower after EART initiation compared to the pre-ART era, with a change in morbidity pattern. Earlier infant diagnosis is needed to initiate ART earlier. The pediatric package of early diagnosis, cotrimoxazole and EART is highly effective in reducing severe morbidity in HIV-infected infants in West-Africa.

No conflict of interest

Abstract: 73

Coinfections in HIV infected children

Yield of community health worker-driven intensified case finding for tuberculosis among HIV-positive in rural Malawi

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Background: Tuberculosis (TB) is the most common cause of death in HIV-positive patients. Prompt diagnosis and initiation of anti-TB treatment (ATT) improves outcomes and minimizes transmission. TB intensified case finding (TB-ICF) among HIV-positive patients is an effective approach endorsed by the World Health Organization however evidence to guide effective implementation in resource-limited settings like Malawi is scarce. The primary objective of this study is to describe the yield of TB-ICF conducted by community health workers (CHWs) among HIV-positive patients accessing antiretroviral therapy (ART) in rural Malawi. Our secondary objective is to describe the burden of TB in this patient population.

Materials & Methods: Thirteen CHWs employed by the Baylor Tingathe outreach program were trained to conduct TB-ICF using a standardized symptom screening tool at a large rural district hospital. Patients were screened while awaiting routine services at ART clinic. Patients screening positive were triaged for assessment by a clinician and sputum analysis by smear microscopy and GeneXpert in parallel. Patients were followed up until final diagnosis and traced if they did not return for their results. CHWs supported patients diagnosed with TB through regular home and facility visits until a final outcome was reached, and screened all household contacts for TB. Sixteen months of pre- and six months of post-intervention data was abstracted from registers and tools used by CHWs during the intervention.

Results: During the pre-intervention period, seven new TB diagnoses were made at ART clinic. Total number screens done was unavailable. During the post-intervention period 459 screens were conducted yielding 46 (10.0%) new TB diagnoses. The number needed to screen per new TB diagnosis was 10. Compared to the pre-intervention period, new TB diagnoses were made at ART clinic during the post-intervention period at a 19-fold higher rate (0.4 vs 7.7 per month). Pediatric TB was only diagnosed in the post-intervention period (9/46, 19.6%). Fourteen patients were already on TB treatment at screening, yielding an observed prevalence of 13.1% (60/459) among screened patients.

Conclusions: These findings suggest using CHWs to conduct TB-ICF is an effective strategy to improve case finding among HIV-positive patients accessing routine care. However it remains unclear if the current rate of case finding will be sustained over time. Future work will focus on the effect of this intervention on patient outcomes.

No conflict of interest
Abstract: 74

Complications of HIV therapy

Intimate partner violence among HIV-infected pregnant women initiating antiretroviral therapy in South Africa

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Introduction: Intimate partner violence (IPV) during pregnancy may be common in settings where HIV is prevalent but there are few data on IPV in populations of HIV-infected pregnant women in southern Africa. We examined the prevalence and predictors of IPV among pregnant women initiating lifelong antiretroviral therapy (ART) in a primary care clinic in Cape Town, South Africa.

Materials & Methods: Participants were consecutive pregnant women seeking antenatal care at a large peri-urban primary care facility. IPV, depression, substance use and psychological distress were assessed using the 13-item World Health Organization Violence Against Women questionnaire, the Edinburgh Postnatal Depression Scale (EPDS), alcohol and drug use disorders identification tests (AUDIT/DUDIT) and the Kessler 10 (K-10) scale, respectively. In analysis, logistic regression was used to examine factors independently associated with experiences of IPV after adjusting for age and socioeconomic status.

Results: From April 2013-May 2014, 623 women were enrolled (median age, 28 years): 38% were married and/or cohabiting and 70% reported not discussing or agreeing on pregnancy intentions prior to conception. Overall, 21% (n=132) reported experiencing ≥1 act of IPV in the past 12 months, including emotional (15%), physical (15%) and sexual violence (2%). Of those reporting any IPV, 48% reported experiencing multiple types. Emotional and physical violence were most prevalent among women 18-24 years old, while sexual violence was most commonly reported among women 25-29 years old. Women who reported not discussing or disagreeing on pregnancy intentions with their partners prior to conception were significantly more likely to experience violence (p=0.030), and women who experienced IPV reported higher levels of substance abuse, depression and emotional distress (p<0.001 for all associations).

Conclusions: These data demonstrate high levels of IPV in this population. While the impact of HIV infection, pregnancy and pregnancy intention on the risk of IPV require further research, IPV screening and support services should be considered as part of the package of routine care for HIV-infected pregnant women.

No conflict of interest

Abstract: 75

Complications of HIV therapy

Changes in Mitochondrial Enzyme Function as a Predictor of Lipodystrophy

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Background: Extended longitudinal data of mitochondrial function in HIV-infected children treated with potent combination antiretroviral therapy (cART) are sparse. We used peripheral blood mononuclear cells to analyze changes in mitochondrial function over a 5-year period. Potential predictors of lipodystrophy were studied.

Materials & Methods: We analyzed data on 38 children enrolled in a clinical trial in Johannesburg, South Africa. All children initiated and were maintained on lopinavir/ritonavir-based cART with viral suppression documented through 5 years of treatment. Buffy coat samples were used for isolation of DNA and analysis of mitochondrial enzyme function. The following markers of mitochondrial function were used: complex IV (CIV) activity (respiratory chain), citrate synthase (CS) activity (mitochondrial mass), the ratios of CIV/CS (respiratory chain function per mass) and mitochondrial to nuclear DNA. DNA measurements were performed by real time PCR. Protein was isolated and function of CIV and CS were assayed by spectrophotometric methods. CD4%, plasma RNA and standardized clinical assessment of lipodystrophy (LD) were documented throughout follow-up.

Results: Fifty-three percent of study participants were female. Age at initiation of cART ranged from 2-23 months (mean 12 months). Median pretreatment CD4% was 15.3 and 54.8% of participants had a plasma RNA > 750,000 copies/ml. Eighteen percent developed lipodystrophy, and 71% (5/7) were female. Mitochondrial DNA (mDNA) increased when pre-treatment values were compared to the 5-year time point. CIV and CS activity increased steadily and had not plateaued after 5 years of treatment. Despite these increases, absolute enzyme function did not reach values seen in uninfected children [CIV (2-3 OD) and CS (10-12 OD)]. Girls (n=20) and those who developed lipodystrophy (n=7) had early, rapid increases CIV activity. Pre-treatment CD4% and plasma RNA did not correlate with enzyme function.

Conclusions: Although continuous recovery in mDNA and absolute enzyme function were observed in these children, they remained below expected levels over 5 years on cART. The more rapid increases in CIV activity observed in those who developed LD, suggests mitochondrial recovery may be involved in evolution of LD.

No conflict of interest

Complications of HIV therapy

Adverse Bone Health among Perinatally HIV-infected Asian Adolescents with Virological Suppression

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Background: Adverse bone health is a long-term complication among perinatally HIV-infected adolescents. Loss of bone mineral deposition during childhood and adolescence may compromise peak bone mass and therefore lead to osteoporosis and fracture later in life. This study aimed to determine the prevalence and associated factors of low bone mineral density (BMD) in perinatally HIV-infected Asian adolescents.

Materials & Methods: A cross-sectional study was conducted at 4 pediatric HIV centers in Thailand (Bangkok [BKK], Chiang Mai [CM], Khon Kaen [KK]) and Indonesia (Jakarta [JK]). Adolescents aged 10-18 years receiving antiretroviral therapy (ART) with virological suppression (plasma HIV RNA <400 copies/mL) were enrolled. Study assessments included
lumbar spine dual-energy X-ray absorptiometry (General Electric-Lunar machine) to evaluate BMD, serum 25-hydroxyvitamin D (25-OHD) and serum biochemical markers for bone remodeling (C-terminal cross-linked telopeptide of type I collagen [CTX] for bone resorption, procolлагen type I amino-terminal propeptide [PINP] for bone formation). BMD Z-score was calculated based on Thai normative age- and sex-matched reference. Low BMD was defined as BMD Z-score ≤-2. Linear regression analysis was conducted to identify factors associated with low BMD. The final model includes age, body mass index (BMI), World Health Organization (WHO) clinical stage prior to ART (stage 4 vs. stage 1-3), boosted protease inhibitor (PI) ever exposure and CD4 percentage prior to ART.

Results: Of 396 adolescents, 57% were female. Median (IQR) age was 15.0 (13.3-16.9) years, and 73% were in Tanner stage 3-5. Median (IQR) duration of ART exposure was 9.3 (6.9-11.5) years, with 40% ever exposed to boosted PIs. Median (IQR) BMD Z-score was -0.7 (95%CI: -1.6 to 0.2). Overall prevalence of BMD Z-score ≤-2 was 16.4% (95%CI: 12.8-20.0%), which varied between sites (CM=23%; BKK=15%; JK=14%; KK=11%; p-value=0.09). In multivariable analysis, boosted PI exposure (mean difference: -0.27; 95%CI: -0.53 to -0.003) and older age (mean difference: -0.17; 95%CI: -0.23 to -0.11) were significantly associated with lower BMD Z-scores. In contrast, higher BMI (mean difference: 0.16; 95%CI: 0.13 to 0.20) and higher CD4 percentage prior to ART (mean difference: 0.03; 95%CI: 0.01 to 0.04) were significantly associated with higher BMD Z-scores. Serum 25-OHD was not associated with lower BMD Z-score (p-value >0.05). The median (IQR) CTX and PINP were 1,270 (860-1,810) ng/L and 337 (153-621) mcg/L, respectively. Both bone remodeling marker levels (CTX: 1,300 vs. 1,270 ng/L; p-value=0.26; PINP: 407 vs.328 mcg/L; p-value=0.44) were not different between adolescents with and without low BMD, respectively. In multivariable model, PINP (per 1% increase in a mean) was significantly inversely correlated with BMD Z-score (mean difference: -0.0023; 95%CI: -0.0041 to -0.0004) while CTX did not show significant correlation (p=0.16).

Conclusions: Low BMD Z-score among perinatally HIV-infected Asian adolescents was documented across sites. Boosted PI exposure, old age, low BMI and low CD4 prior to initiation of ART were associated with adverse bone health. Dysregulation of bone formation process may reflect the disturbance of bone remodeling which is the underlying mechanism of bone demineralization. The interventions to prevent further bone loss and improve bone health for this population are definitely required.

No conflict of interest

Abstract: 77

Complications of HIV therapy

Dysregulated Bone Remodeling but Stable Bone Mineral Density over 4-year Tenofovir Disoproxil Fumarate Exposure among Perinatally HIV-infected Asian Adolescents

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Background: Tenofovir disoproxil fumarate (TDF) is widely used as a backbone in combination antiretroviral therapy (ART) regimens for HIV-infected adults and adolescents. Whether long term use of TDF impairs bone mineral accrual in HIV-infected adolescents is controversial. This study aimed to determine the effects of TDF on bone mineral density (BMD) and bone remodeling regulation in Asian adolescents with perinatally acquired HIV infection.

Materials & Methods: A case-control study was nested within a cohort of 396 HIV-infected HIV-infected...
Asian adolescents from 4 pediatric HIV centers in Thailand (Bangkok, Chiang Mai, Khon Kaen) and Indonesia (Jakarta). Adolescents aged 10-18 years with virological suppression (plasma HIV RNA<400 copies/mL) were enrolled. Individuals exposed to TDF for at least 3 months were identified as case, while individuals never exposed to TDF were controls. Study assessments included lumbar spine dual-energy X-ray absorptiometry (General Electric-Lunar machine) to evaluate BMD and serum biochemical markers for bone remodeling (bone resorption: C-terminal cross-linked telopeptide of type I collagen [CTX]; bone formation: procollagen type I amino-terminal propeptide [PINP]). BMD Z-score was calculated using age- and sex-matched healthy Thai adolescents as a reference. Median BMD Z-scores across each additional year of TDF exposure were compared using test of trend. Linear regression analysis was performed to determine the association of TDF use and each biochemical marker for bone remodeling.

Results: There were 138 adolescents who had exposed to TDF with a median (IQR) duration of 2.3 (1.4-3.1) years and 257 adolescents in control group. Adolescents with TDF exposure were older (16.1 vs. 14.3 years; p-value <0.001), had more advanced Tanner stage (proportion of Tanner stage 3-5: 90% vs. 65%, p-value <0.001) than controls. Additionally, TDF-exposed group had longer duration of ART use (10.6 vs. 8.7 years; p-value <0.001), higher proportion of boosted protease inhibitor use (59% vs. 30%, p-value<0.001), and higher CD4 percentage prior to ART initiation (16% vs. 11%, p-value = 0.04), compared with control group. There was no difference in median BMD Z-scores among TDF-exposed and unexposed groups (-0.8 vs -0.6, p-value = 0.23). Comparing adolescents with different TDF exposure time (non-exposed, 1 to 4 years), there was no significant different in BMD Z-score across groups (-0.6 vs. -1.2 vs. -0.7 vs. -1.0 vs. -0.9, respectively; p-value for trend = 0.29). In multivariable analysis, TDF exposure was significantly positively associated with CTX-bone resorption marker (mean difference: 127.7 ng/L; 95%CI: 5.9 to 249.4) and negatively associated with PINP-bone formation marker (mean difference: -64.4 mcg/L; 95%CI: -128.1 to -0.8), adjusted for gender and body mass index.

Conclusions: Even though, the dysregulation of bone remodeling was observed, there was no significant difference in BMD among HIV-infected adolescents with varied TDF exposure duration over 4-year period. These individuals may be able to keep net balance of bone remodeling process, and thus no adverse bone outcome was demonstrated.

No conflict of interest

Abstract: 78

Complications of HIV therapy

Higher 25-hydroxyvitamin D levels in perinatally HIV-infected Asian adolescents receiving boosted protease inhibitors

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Background: Vitamin D deficiency (VDD) is associated with a number of adverse health outcomes. High prevalence of VDD has been reported among HIV-infected individuals, mostly from Western countries. This study aimed to investigate the prevalence of VDD and its associated factors among perinatally HIV-infected Asian adolescents receiving antiretroviral therapy (ART).

Materials & Methods: A cross-sectional study was conducted at 4 referral pediatric HIV centers in Thailand (Bangkok [BK], Chiang Mai [CM], Khon Kaen [KK]) and Indonesia (Jakarta [JK]). Adolescents aged 10-18 years receiving ART with virological suppression (plasma HIV RNA <400 copies/mL) were enrolled. Data on demographics, history and current ART regimen, ART duration, CD4 and plasma HIV

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RNA were collected. Duration of sun exposure (hours/day) and physical activity levels (score 1 [low activity] to 5 [high activity]) were assessed using standardized questionnaires. Laboratory evaluations included serum 25-hydroxyvitamin D (25-OHD) and intact parathyroid hormone (iPTH) levels. VDD was defined as a 25OHD levels <20 ng/mL. Linear regression analysis was performed to identify factors associated with VDD. The final model includes sex, body mass index (BMI), physical activity scores, current ART regimens (boosted protease inhibitors [PIs] versus non-nucleoside reverse transcriptase inhibitors [NNRTIs]), current CD4 cells count and iPTH levels.

Results: During April to December 2014, 394 adolescents were enrolled, 57% were female, and median (IQR) age was 15.0 (13.3-16.9) years. Median (IQR) duration of ART and current CD4 cell count were 9.3 (6.9-11.5) years and 734 (581-907) cells/mm³, respectively. One-hundred forty (37%) adolescents currently received PI-based regimens, mostly (81%) were lopinavir/ritonavir, with a median (IQR) duration of 7.0 (4.3-9.9) years. Two-hundred and thirty-four (61%) adolescents received NNRTI-based regimens, of which 114 (49%) and 120 (51%) were efavirenz and nevirapine, respectively. Median (IQR) duration of sun exposure and physical activity scores were 0.4 (0.2-0.8) hours/day and 1.8 (1.4-2.5), respectively. Median (IQR) 25-OHD level was 26.3 (20.8-32.9) ng/mL. Overall prevalence of VDD was 21% (95%CI: 17-25%), which varied across sites (JK = 41%; CM = 28%; BKK = 20%; KK = 10%; p-value = 0.001), only 8 (2%) had severe VDD (serum 25-OHD <10 ng/mL). Shorter duration of sun exposure was observed among JK compared with Thai adolescents (0.29 vs. 0.41 hours/day, p-value = 0.23). In multivariable analysis, boosted PI regimen (mean difference: 3.6 ng/mL; 95%CI: 1.6-5.6) was significantly associated with higher 25-OHD levels. In contrast, female sex (mean difference: -4.8 ng/mL; 95%CI: -6.8 to -2.8) and higher BMI (mean difference: -0.3 ng/mL; 95%CI: -0.6 to -0.02) were significantly associated with decreased 25-OHD levels. Intact PTH was negatively correlated with 25-OHD levels (mean difference: -0.08; 95%CI: -0.13 to -0.04), while the correlation between EFV exposure and 25-OHD status was not demonstrated in this study (p-value >0.05).

Conclusions: Approximately one-fourth of perinatally HIV-infected adolescents have VDD. Boosted PIs may impair vitamin D bioactivation to 1,25-dihydroxyvitamin D, and thus increase 25-OHD levels.

No conflict of interest

Abstract: 79

Complications of HIV therapy

Maternal tenofovir disoproxil fumarate (TDF) use in pregnancy not associated with adverse growth outcomes at 6 weeks and 9 months among Kenyan HIV-exposed uninfected infants

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Introduction: Tenofovir disoproxil fumarate (TDF) is commonly used in antiretroviral treatment (ART) and in pre-exposure prophylaxis (PrEP) regimens. Accruing TDF safety data among infants exposed to TDF in pregnancy is important, especially in sub-Saharan African settings.

Materials & Methods: Data from a cross-sectional survey of mother-infant pairs conducted July-December 2013 in 140 maternal child health clinics throughout Kenya were analyzed to evaluate the relationship of maternal TDF use in pregnancy and growth outcomes among infants with PCR-confirmed HIV-negative status. Maternal ART regimen during pregnancy and birth information was determined by self-report and confirmed with clinic records. Anthropometric measurements from infants attending 6-week or 9-month immunization visits were assessed by mobile evaluation teams. Age & sex-adjusted z-scores for weight (WAZ), weight-for-length (WLZ), length (LAZ), and head circumference (HCAZ)
were calculated using WHO Child Growth Standards and analyzed as continuous variables. Comparisons of HIV-exposed uninfected (HEU) infants with and without TDF exposure were assessed using t-tests and multivariate linear regression models adjusted for maternal and infant demographic and medical characteristics accounting for clinic-level clustering.

Results: Overall, 277 HEU infants had mothers who used three-drug combination ART during pregnancy, of whom 63% initiated ART before pregnancy and 89 (32%) used TDF-containing regimens. Prenatal TDF use was associated with concurrent use of protease inhibitors (26% vs 7%, p<0.001) and with WHO clinical stage III (14% vs 6%, p=0.030). No differences in birth weight (3.0 kg vs 3.1 kg, p=0.205) or gestational age at birth (38 weeks vs 38 weeks, p=0.160) were detected between TDF-exposed and unexposed infants. Mean WAZ at 6 weeks was lower among TDF-exposed infants in unadjusted comparison (-0.8 vs -0.4, p=0.033); the association was less significant in adjusted analyses, (p=0.057). There were no associations between maternal prenatal TDF use and WLZ (p=0.509), LAZ (p=0.998) and HCAZ (p=0.964) among infants in the 6-week postpartum cohort. Among infants attending 9-month visits, no association was detected between maternal prenatal TDF use and WAZ (p=0.349), WLZ (p=0.655), LAZ (p=0.514) and HCAZ (p=0.888) after adjustment.

Conclusions: Our results add to previous data suggesting that maternal TDF use during pregnancy is not associated with adverse infant growth outcomes compared to non-TDF ART use.

No conflict of interest

Abstract: 80

Complications of HIV therapy

Neurocognitive Outcomes in Pre-School and Early School-Age HIV-Exposed Uninfected Children Exposed Pre- or Perinatally to Antiretroviral Medications

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Background: The nucleoside reverse transcriptase inhibitors alter mitochondrial replication and function. Since brain development requires energy, medications affecting mitochondrial energy production during fetal life and infancy could affect brain development. Studies of infants and toddlers suggest no effect of pre- and peri-natal antiretroviral drug exposure (ARV) on early cognitive and adaptive function, but little is known about longer-term outcomes. We report here on neurodevelopmental outcomes of 3 to 6 year old HIV-exposed uninfected (HEU) children exposed in utero and perinatally to ARVs, in comparison to a sociodemographically matched control group.

Materials & Methods: HEU children underwent neurodevelopmental assessments as part of routine care in the SickKids Family-Centred HIV Clinic. A control group was recruited in the communities where the HEU children are known to live. Children were administered standardized tests of intelligence and the Vineland Adaptive Behaviour Scales. Children were divided into two groups: mean age 3.5 years and 5.5 years.

Results: 110 children (74 HEU, 37 controls) were assessed. Their families were from an ethnically diverse, largely immigrant background, with maternal country of origin being Africa (32% HEU, 24% Controls), Canada (28% HEU, 24% Control), the Caribbean (23%
HEU, 27% Control), South/Southeast Asia (11% HEU, 16% Control); and South America (5% HEU, 8% Control). There were no group differences in birth weight, gestational age, and maternal education or employment status. At age 3.5, the HEU and control groups did not differ on IQ, but the HEU children had significantly lower adaptive function. The 5.5-year-olds differed from controls on IQ and adaptive function.

Conclusions: Adaptive skills were reduced at both ages in ARV-exposed children. Differences in intelligence emerge with increased age, highlighting the importance of examining long term development. It remains to be determined whether cognition worsens and whether other deficits appear with increased age. These findings need replication in larger samples.

No conflict of interest

Abstract: 81

Complications of HIV therapy

Socio-demographic and clinical predictors of preterm births, low infant birth weight, and pregnancy complications among women living with HIV (WLWH) in Ontario, Canada

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Background: Pregnancies amongst WLWH are increasing as a result of advances in combination antiretroviral therapy and the increasing proportion of WLWH of childbearing age. These women are also at increased risk of adverse obstetric outcomes. This study examined socio-demographic and clinical characteristics as correlates of premature birth (PB), low birth weight (LBW), and pregnancy complications (PC).

Materials & Methods: The HIV Mothering Study is an observational mixed methods study exploring psychosocial experiences and needs of mothers living with HIV in Ontario. Data during the 3rd trimester of pregnancy and at 3 months postpartum was obtained through surveys and medical records. The UCLA Loneliness, HIV Stigma, Everyday Discrimination-Racism, and Medical Outcomes Study-Social Support Survey scales were used for psychosocial assessments. We employed the penalized-maximum likelihood logistic regression to eliminate small-sample bias and stepwise regressions to create final multivariate models. For each of the outcomes, covariates with p-values < 0.20 were included, followed by backward elimination of covariates until best-fit models were reached.

Results: Of the seventy-six women in this analysis, eight deliveries were PB, eleven were LBW, and fourteen PCs were encountered (e.g. pre-eclampsia, gestational diabetes, antepartum hemorrhage; feet/hand swelling, prolonged vomiting). Having a CD4 count higher than 500 cells/mm³ correlated with a reduced chance of PB (OR=0.01; p=0.002), while history of cardiovascular disease increased the risk (OR=35.77; p=0.005). Interestingly, higher risk for LBW was found to be associated with prepartum depression (OR=24.81; p=0.014), divorce/separation (OR=32.50; p=0.024), and reduced social support (OR=0.92; p=0.018). The strongest correlates of both delivery outcomes, PB and LBW, was having CD4 count lower than 200 cells/mm³ (OR=10.57; p=0.049) and depression (OR=0.21; p=0.016). As for maternal PCs, the significant correlates were low CD4 count (OR=0.004; p=0.004), use of protease inhibitors (OR=0.13; p=0.025), and experience of racism (OR=1.18; p=0.036).
Conclusions: Low CD4 count, history of cardiovascular disease, depression, marital status, use of protease inhibitors, social support, and racism can elevate the risk of adverse obstetric outcomes and pregnancy complications for pregnant WLWH. Specific strategies addressing these clinical and socio-demographic risk factors should be adopted prior to delivery in order to improve health trajectories for both mother and child.

No conflict of interest

Abstract: 82

Implementation research on PMTCT and pediatric treatment programs

Option B+ for prevention of mother-to-child HIV transmission: Healthcare worker perspectives

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Background: The Ministry of Health (MOH) in the Kingdom of Swaziland has partnered with ICAP at Columbia University to implement a USAID-funded implementation science study to evaluate Option B+, a prevention of mother-to-child transmission (PMTCT) approach in which all HIV+ pregnant and breastfeeding women initiate lifelong antiretroviral therapy (ART) independent of CD4+ count. Healthcare workers (HCW) are critical to the successful implementation of Option B+, yet little is known about acceptability of the Option B+ approach among HCWs.

Materials & Methods: From August 2013 through May 2014, ten health facilities across the Manzini and Lubombo regions in Swaziland transitioned from Option A, the standard of care for PMTCT, to Option B+. One or more nurses at each site were trained in ART management prior to Option B+ transition. HCWs received intensive onsite training throughout the transition to Option B+ including the introduction of a comprehensive Option B+ counseling flipchart. Five HCWs from each health facility (N=50) completed in-person surveys, consisting of closed- and open-ended questions, to assess Option B+ feasibility and acceptability at the time of transition and again two months after Option B+ implementation.

Results: Participants included nurses/nurse midwives (58%), mentor mothers (14%), expert clients (12%), peer counselors (10%), and adherence officers (4%). Nearly half (48%) of HCWs cited immediate ART initiation as a primary advantage of Option B+, reporting that it simplified the process for HCWs and patients by reducing delays from tests or labs and eliminating eligibility requirements and wait times for ART. Twenty-six percent of HCWs reported that Option B+ included stronger and more comprehensive counseling sessions than Option A and 18% reported that Option B+ streamlined follow-up and counseling procedures. Thirty-four percent of HCWs reported increased patient ease and acceptance of PMTCT due to the simplified medication regimen of the Option B+ approach. Fewer HCWs cited lack of coordination between services (requiring women to visit multiple service points) as a barrier to PMTCT uptake under Option B+ (40% of HCWs) compared to Option A (54% of HCWs), suggesting increased integration of services under Option B+. Seventy percent of HCWs reported that same-day ART initiation under Option B+ may introduce new patient-level barriers to acceptability for patients who may be hesitant to start treatment, citing at least one of the following barriers to same-day ART initiation: disclosure/partner consultation, lack of familiarity/acceptability of Option A, and/or reluctance to initiate life-long treatment. Over half (64%) of HCWs felt they performed more work under Option B+, specifically reporting increased involvement in HIV, CD4, and PCR testing, counseling, prescribing/monitoring medications, and appointment scheduling/tracking. Nearly all HCWs (98%) believed that all HIV+ pregnant women should start ART and continue treatment for life (Option B+).

Conclusions: As Swaziland rolls out Option B+ nationally, study findings demonstrate HCWs view Option B+ as an acceptable and feasible PMTCT approach. Additional research is
necessary to determine strategies to address potential barriers to patient acceptability and assess the longer term views of HCWs.

No conflict of interest

Abstract: 83

Implementation research on PMTCT and pediatric treatment programs

Optimizing Health Information Systems for Option B+ in Swaziland

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Introduction: The Option B+ approach for prevention of mother-to-child transmission (PMTCT) of HIV presents opportunities for streamlined treatment and retention for mothers and their infants. However, paper-based health information systems (HIS) are often redundant and poorly integrated across maternal-infant care. We examined documentation protocols and their implementation in the context of PMTCT.

Material & Methods: ‘Situkulwane Lesiphephile—Safe Generations’ is an implementation science research study evaluating Option B+ outcomes in the Kingdom of Swaziland using routinely collected patient-level data. Facility and healthcare worker assessments were conducted at 10 PMTCT clinics to identify and describe PMTCT service documentation under Option B+. Documentation source was tabulated against visit type, maternal and infant health indicators, and maternal and infant unique identifiers to evaluate: a) proportion of repeated data collected across documentation source, b) the burden of documentation at each visit type, and c) the presence or absence of maternal-infant linking through unique identifiers.

Results: Swaziland PMTCT HIS includes 12 documentation sources for maternal data and 4 sources for infant data. Multiple paper-based documentation sources are completed for each PMTCT visit (min 10, max 15). Many indicators are duplicated across these sources. For example, health workers must document maternal HIV status on eight separate forms for each PMTCT visit. Maternal HIV status is the only key variable routinely recorded on infant documentation sources; maternal health and treatment status are not found on any infant record. Unique identifiers are not used to link maternal-infant pairs on any documentation source. Healthcare workers report an increased burden of documentation with integration of ART into ANC services and fail to routinely document all information on all forms at each visit. For example, no CD4+ count and no birth date were recorded for 17% and 16% of women, respectively, across all documentation sources.

Conclusions: The multitude and replication of maternal and infant documentation required for a single PMTCT visit burdens healthcare workers and increases risk for inconsistent, erroneous, and incomplete data. New approaches to Option B+ documentation, including introduction of electronic medical records, are urgently needed to facilitate and accurately record maternal-child health service delivery and PMTCT outcomes.

No conflict of interest

Abstract: 84

Prevention of Mother-to-Child transmission

Why Did I Stop? Barriers and Facilitators to Acceptance of and Retention in the Option B+Program in Lilongwe, Malawi

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Introduction: Despite the early success of Malawi’s Option B+ program, early loss to follow-up remains a challenge. Few studies address how women make treatment decisions and their reasons for dropping out of care. This study compares the experiences of women in care and those not in care and examines how women decide whether to start and stay on ART. We aim to identify the key factors that lead to ART refusal, default, and retention.

Materials and Methods: We conducted in-depth qualitative interviews with HIV positive women who initiated ART through Option B+ in Lilongwe, Malawi (N=62). We included those successfully retained in care (N=27) and those who refused/defaulted ART (N= refuse14; default 21). Open ended interviews were used to understand women's experience through the PMTCT cascade. We explored potential barriers and facilitators to acceptance/retention in Option B+. Data was analyzed in Atlas.ti using an inductive approach based on grounded theory methodology.

Results: Women who refused ART were concerned with immediate initiation. Half of the women who refused felt healthy and wanted to wait until their health declined or try alternate forms of healing first (7/14). Others expressed that they wanted to wait because they needed time to process their newfound status (4/14). The main reasons women gave for defaulting includes side effects and lack of partner support. 43% of women expressed that the severity of efavirenz related side effects were too much to bear (9/21). 29% expressed that their husbands were not supportive and was preventing them from taking their treatment (6/21). The most common reason women gave for accepting ART was to protect their child and future health (16/27). Several women felt sick when tested positive and saw ART as the way to become healthy again (7/27). In general, we found that treatment decisions were considered an individual's own decision (44/62). Partners, family, community, and church members’ opinions were noted but did not determine a woman's choice to start or stop ART.

Conclusions: Successful retention is related to how women conceptualize early ART initiation in light of their perceived health. Interventions that provide early support for patients experiencing side effects may be helpful.

No conflict of interest

Abstract: 85

Prevention of Mother-to-Child transmission

Kenya rolls out option B plus towards elimination of mother to child transmission of HIV

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Introduction: According to Kenya AIDS Indicator Survey (KAIS) 2012, 1.2 million (5.6%) people live with HIV/AIDS. Of these, 106,000 were newly infected previous year. Globally Kenya is ranked among 22 priority countries targeted to reduce new HIV infections in children. Approximately101, 000 (0.9%) children between 18mo-14 years are HIV-infected, majority due to mother to child transmission. In 2013 WHO recommended use of HAART for all HIV positive pregnant and lactating women; guideline adopted by Kenya in October 2013.

Materials & Methods: Dissemination of national guidelines was done by National AIDS Control Program assisted by implementing partners. There was nationwide rollout of option B plus starting with large volume facilities offering ART and facilities which already integrated HAART within MCH. USAID APHIAPLUS Kamili scaled up Option B plus to 134 high volume facilities in Eastern and Central Kenya. County Health Managers and serviceproviders were oriented on new guidelines. Regular supervision, mentorship, routine chart reviews and HIV-exposed infant cohort analysis was established. HIV positive mentor mothers were recruited and placed in high volume facilities, to support adherence and retention in care of HIV positive pregnant mothers. HAART was integrated into MCH for
easy access. Exclusive breastfeeding for 6 months was encouraged. National EID website was monitored for PCR results.

**Results:** During the period October 2013 to September 2014 (Annual Progress Report - APR 2014), a total of 1,320,664 pregnant women had known HIV status of whom 66,258 (5%) were HIV positive. Of those positive, 56,137 (85%) were put on ARV prophylaxis. Of those on prophylaxis, 64.2% were on HAART for life (Option B plus). For KAMILI supported zone, EID positivity reduced between APR 2013 and 2014 as follows: @2mo from 5.9% to 4.8%; @9mo from 7.5% to 6.2%; @12mo from 7.8% to 6.7%; @18mo from 8.7% to 7.5%. Nationally 6 weeks PCR positivity has dropped as follows: 12% (2010); 10% (2011) ; 6% (2012) ; 5% (2013); 4% (2014).

**Conclusions:** Introduction of Option B plus in Kenya has contributed to further reduction in mother to child transmission of HIV, leading to achievement of Kenya's goal of virtual elimination (transmission <5%) by 2015. Exclusive breastfeeding for 6 months, use of mentor mothers and integration of HAART within MCH are key success factors.

No conflict of interest

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**Abstract:** 86

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

**Achieving elimination of mother-to-child transmission of HIV in low and concentrated epidemics: an analysis on health and cost outcomes of universal versus targeted approach**

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**Introduction:** Significant progress has been made towards eliminating mother-to-child transmission of HIV (MTCT) with expanded HIV testing and counselling in antenatal care (ANC) settings. As HIV resources decrease, countries with low HIV prevalence are exploring ways to target their approaches on prevention of mother-to-child transmission of HIV (PMTCT). We examined universal provider–initiated testing and counselling (PITC) versus geographically targeted testing for pregnant women in low and concentrated HIV epidemics in order to provide evidence for future guidance.

**Materials & Methods:** A modelling analysis on health and cost outcomes of PMTCT was conducted using the Costing Tool for Elimination Initiative (CTEI). Based on the country case study, several scenarios on universal and targeted approaches were examined for Country A, which we assumed to have 1,000,000 annual births, HIV prevalence of 0.4%, ANC coverage of 90%, and HIV testing coverage of 50%. The country was divided into three categories based on HIV prevalence; high burden provinces with HIV prevalence of 0.6%; intermediate burden with prevalence of 0.4%; and low burden with prevalence of 0.05%. Sensitivity analysis was conducted on major variables.

**Results:** The analysis of the universal approach with a sensitivity analysis varying HIV prevalence between 0.9% and 0.01%, confirmed that PMTCT with universal testing was cost saving by averting new HIV infections among children and thus reducing the cost of paediatric HIV treatment in the future even with HIV prevalence levels of less than 0.1%. Scenario analysis on targeted approaches found that it could yield similar results to the universal approach in which a population MTCT rate of 7% could be achieved with improved service coverage of 95% in both high and intermediate burden provinces. In contrast, the highly targeted approach which focused only on high burden provinces was not as effective as a targeted approach which included both high and intermediate burden provinces, and failed to reduce MTCT rate to less than 16% in our analysis. Cost of PMTCT services and cost per infection averted were similar across scenarios.
Conclusions: The universal approach is preferable when striving towards elimination of new paediatric HIV infections and also saves future paediatric treatment costs. While identifying resources, a targeted approach could be applied in the interim provided that thorough scenario analysis using reliable subnational data for effective targeting has been conducted.

No conflict of interest

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Prevention of Mother-to-Child transmission

Contributors to high HIV transmission among HIV exposed infants at a hospital implementing option B plus in Uganda

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Background: Uganda launched Option B+ in December 2012. Studies conducted in Africa report varying risk factors for Mother to Child Transmission of HIV (MTCT) including maternal and infant factors. Antiretroviral therapy (ART) during breastfeeding reduces transmission to 1%-5% but neither infant nor maternal postpartum ART prophylaxis completely eliminates risk of HIV transmission via human milk. Despite implementation of Option B plus and ART coverage of 90% among HIV positive women in antenatal clinic, national MTCT rates continue to be at 6.5%. Furthermore, the HIV transmission rate from mother to infant is highest among children attending Jinja Hospital 16% compared to average of other Regional Referral Hospitals at 8%. This study was conducted to assess factors associated with HIV transmission among HIV exposed infants attending Jinja Regional Referral Hospital.

Materials & Methods: A Retrospective Case Control study conducted at Jinja Regional Referral Hospital, Uganda among infants born to HIV positive mothers registered at Early Infant Diagnosis clinic from April 2013 to December 2014. Cases were HIV-positive infants and controls were HIV Negative infants. Data was collected using data abstraction and interviewer administered questionnaire including socio-demographic characteristics of infant and caretakers and risk factors associated with HIV infection.

Results: A total of 80 caretakers were interviewed. There were forty cases and forty controls aged between 3 to 24 months. Fifty percent of infants were male, 88% of mothers delivered either in a private (27%) or public hospital (61%), 31% did not attend ANC and 30% of caretakers had unknown HIV serostatus during pregnancy. Factors associated with HIV transmission were Mixed feeding at 3 months OR 9 CI 2.7-3 p=0.00, baby not receiving nevirapine OR 6.2 CI 2.4-16.5 p=0.00, mother not attending ANC OR 8.9 CI 1.4-10.8 p=0.01, receiving infant feeding counseling OR=6.7, CI=4.9-56.6, p=0.00, delivering at a government facility OR=3 CI=1.3-8.6 P=0.02, mother did not use ART during pregnancy OR 8.1 CI 3-21.9 p=0.00. Using Option B plus was protective 0.34 CI 0.2-0.7, p=0.00.

Conclusions: Commitment to virtual elimination of HIV remains a challenge unless there is improvement on ANC attendance, HIV testing and use of ART, hospital delivery and infant feeding counselling.

No conflict of interest

Abstract: 88

Prevention of Mother-to-Child transmission

Optimizing Zimbabwe's National PMTCT Program: Cost-effectiveness of a village based intervention to improve mother-infant linkage to postnatal care
Abstract

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Introduction: Low retention of mother-infant pairs in postnatal care (PNC) reduces the effectiveness of PMTCT programs offering Option B+ (lifelong ART). We projected the clinical and economic impact of a planned village health worker (VHW)-based intervention to re-engage mother-infant pairs who fail to link to PNC after delivery in Zimbabwe.

Materials & Methods: Using the Cost-effectiveness of Preventing AIDS Complications (CEPAC) model, we simulated a cohort of Zimbabwean women identified as HIV-infected and treated with ART during antenatal care and their infants (mean maternal age: 24 years, CD4: 451/μL, breastfeeding duration: 18 months). We compared three strategies: no PMTCT program (comparator), current national program, and current program plus a VHW-based intervention to identify and re-engage in care mother-infant pairs who fail to link to PNC by 6 weeks postpartum. Based on program and published data, we modelled successful 6-week PNC linkage (current: 43%; current+VHW: 71.5%; 50% of traced defaulters linked); VHW program costs were US$35/mother-infant pair traced. Model outcomes included mother to child transmission (MTCT) risk, maternal and pediatric life expectancy (LE), and lifetime healthcare costs (2013 US$). We calculated incremental cost-effectiveness ratios (ICERs) in US$/life-year saved (US$/LYS) from discounted maternal+pEDIATRIC LE and costs, defining ‘very cost-effective’ as ICER per-capita GDP). Sensitivity analyses varied intervention effectiveness, intervention costs, and loss to follow-up after initial linkage to PNC (late-LTFU).

Results: Compared to no PMTCT, the current national program was projected to reduce MTCT from 26.0% to 8.8%, increase pediatric LE from 48.70 to 57.37 years, and be cost-saving. The VHW program further reduced projected MTCT risk to 7.2% and increased maternal and pediatric LE (by 1.9 and 0.8 years). The VHW program increased total projected lifetime costs - including healthcare and ART costs - by $510/mother-infant pair, but was very cost-effective (ICER US$350/LYS vs. current program). It remained very cost-effective through wide variations in cost and effectiveness. With high late-LTFU, many clinical benefits were lost.

Conclusions: VHW-based interventions to improve linkage to PNC will provide good value for investment in Zimbabwe. Long-term retention of mother-infant pairs in care is critical to realize these benefits and optimize outcomes of Option B+ implementation in Zimbabwe.

No conflict of interest

Abstract: 89

Prevention of Mother-to-Child transmission

Effectiveness of Lifelong Antiretroviral Therapy for HIV-positive Pregnant and Lactating Mothers on Elimination of Mother to Child Transmission of HIV in Uganda.

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Background: In Uganda, vertical transmission of HIV from mother to child is the second common route of transmission, accounting for 18% of all new infections. The country is a signatory to the global plan for virtual elimination of new HIV infections among children. The target is to reduce mother-to-child transmission (MTCT) of HIV to less than 5% by 2015. To achieve this target, lifelong combination antiretroviral therapy (ART) to HIV-positive pregnant and lactating mothers (option B+) was rolled out in Uganda in October 2012.
We examined the effectiveness of the option B+ strategy on reducing MTCT among babies born to HIV-positive mothers.

Materials & Methods: This was a retrospective cohort analysis of data abstracted from health facility records of 1,129 mother-baby pairs (HIV-infected mothers and their exposed babies) enrolled on lifelong combination antiretroviral therapy between January and March 2013 at 145 health facilities in 24 districts of central Uganda. The MTCT rates at 6 weeks [at 1st Polymerase Chain Reaction (PCR) test] and at 18 months (final rapid HIV test) post-partum were calculated. These were compared with the mother’s socio-demographics, place of delivery, health facility level, CD4 cell count at ART initiation, adherence to ARVs, infant feeding practices and the infant ARVs prescribed using the Cox proportional hazard model.

Results: The mother’s median age was 25 years (IQR, 22-29). The majority 1,095 (97.0%) were initiated on Tenofovir / Lamivudine / Efavirenz (TDF/3TC/EFV) ART regimen. The median CD4 count at ART initiation was 524 cells/µl (IQR, 346-736 cells/µl). Good adherence to ARVs (taking ≥ 95% of the prescribed tablets) was registered in 796 (70.5%) mothers. The infants’ median age at 1st PCR test was 1.5 months (IQR, 1.5-2) and that at final HIV test was 21.1 months (IQR, 19.1-23.7). The MTCT rate at 1st PCR was 3.2/100 Person Months (PM) (95% CI 2.4-4.3) while that at final HIV rapid test was 4.4/100 PM (95% CI 3.3-5.8). Maternal poor adherence to ARVs (taking < 75% of the prescribed tablets) [Adjusted Hazard Ratio (AHR) 1.89 (95% CI 1.30-2.73)] and having no ARVs prescribed for the babies (AHR 1.22 (95% CI 1.03-1.45)] were associated with MTCT of HIV.

Conclusion: These findings suggest that lifelong combination ART is an effective strategy for reducing MTCT of HIV. Interventions for improving adherence to ART among HIV-positive pregnant and lactating mothers are needed. The need to prescribe ARVs for prophylaxis for all HIV-exposed babies is critical

No conflict of interest

Abstract: 90

Prevention of Mother-to-Child transmission

Lack of standardized measurement in early retention monitoring may obscure PMTCT program successes

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Background: Despite the successes of enrolling HIV-infected pregnant and breastfeeding women in treatment under lifelong ART (Option B+), retaining them in care poses persistent challenges. Monitoring early ART retention is important for individual health outcomes and program effectiveness. Currently there is no recognized standard definition for retention in PMTCT care. We compared six month retention using 4 commonly applied measurement approaches.

Materials & Methods: Retrospective patient level data on monthly clinic attendance (M1-M7) were collected from HIV clinic registers at a random sample of 186 health facilities in Uganda. All pregnant and breastfeeding women newly initiating ART from October-December 2013 were included. Retention was defined using four approaches: 1) attending a clinic visit within the 90 days prior to the 6 month visit; 2) attending a clinic visit within a thirty day window before or after the 6 month visit; 3) completing a visit in month six after ART initiation; and 4) attending all clinic visits up to and including the 6 month visit. Patient-level retention was calculated using each definition and compared using McNemar’s Test. Chi-square tests were used to test the associations between retention and other categorical variables.

Results: A total of 165 sites contributing 1869 patients were included. The six month retention using definition (1), the most commonly used measure, was 72.4% (95%CI: 70.4-74.5%);
70.5% (95% CI: 68.5-72.6%) using definition (2); 60.9% (95% CI: 59.7-64.1%) using definition (3); and 42.9% (95% CI: 40.7-45.1%) using definition (4). Retention estimates were significantly different across all comparisons. (p<0.0001). Overall, 288 (15.2%) women never returned to care after their first visit when ART was initiated. Adherence to monthly visit schedule varied by health facility type (p<0.001), with referral hospitals having the largest proportion of patients failing to attend a second visit after ART initiation (22.2%) compared to primary health centers (8.8%).

Conclusions: Accurately measuring PMTCT program effectiveness and ultimately impact on MTCT requires reliable measurements of retention in care. Significant variability was observed among the measures used to categorize patients as retained. Lack of standardized retention definitions and measurement approaches not only limits comparability of retention within and across country programs but may also obscure early maternal retention.

No conflict of interest

Abstract: 91

Prevention of Mother-to-Child transmission

Use of combination neonatal post-exposure prophylaxis for prevention of vertical transmission of HIV in the Canadian Perinatal HIV Surveillance Program (CPHSP) 1997-2014

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Background: Combination neonatal antiretroviral prophylaxis (cART) has been used in high-risk situations in Canada to prevent vertical transmission of HIV (VT), despite limited data supporting its use, and little consensus on optimal antiretroviral regimens and dosing for this indication. The objective of this study was to describe the use of cART as prophylaxis in neonates in Canada.

Materials & Methods: All HIV-exposed newborns in Canada born between 1997-2014 were identified from the Canadian Perinatal HIV Surveillance Program, a federal program collecting maternal and newborn data on HIV transmission during pregnancy. Neonatal prophylaxis was categorized as single, 2 or 3-drug regimens and further sub-categorized by specific treatment type. Factors associated with prescription of cART (³3 drugs) were determined by logistic regression.

Results: Between 1997-2014 (n=3200), 64.5% of newborns received only zidovudine (ZDV), 17.7% received a two-drug combination (10.6% ZDV and Lamivudine (3TC), 6.9% ZDV and 1-3 doses of nevirapine (NVP), and 0.2% other), and 15.0% received cART (10.5% ZDV, 3TC and a protease inhibitor, 2.4% ZDV, 3TC and 4 weeks of continuous NVP, and 1.8% ZDV, 3TC and 1-3 doses of NVP). The peak of cART prescriptions occurred in 2002, when 29.0% of all HIV exposed newborns in Canada received triple-drug prophylaxis; this decreased to 7.0% in 2014. Factors associated with the prescription of cART (2008-2013) included no maternal antenatal treatment vs. maternal cART (OR: 13.5, 95% CI 7.90-23.40), duration of maternal therapy <4 vs. >4 weeks (OR 24.5, 95% CI 12.0-50.0), suboptimal vs. excellent adherence (OR: 39.9, 95% CI 18.2-87.1), no-intrapartum vs. intrapartum ZDV (OR 2.95, 95% CI 1.83-4.75), and region (eastern vs. western Canada, OR 4.05, 95% CI 1.46-11.23). The VT rate in cART-treated infants was 4.15%.

Conclusions: While cART has been used for neonatal prophylaxis in Canada since 1998, there is considerable heterogeneity in regimens used, and prescribing practices across provinces. Further work is needed to identify the
safest and most effective cART regimens for newborns at high risk of VT.

This data has been presented in part at the Canadian Association for HIV Research (CAHR) Annual Meeting, Toronto, Ontario, May 1st 2014.

No conflict of interest

Abstract: 92

Prevention of Mother-to-Child transmission

Immediate initiation of antiretroviral therapy in PMTCT programmes is not associated with non-adherence during pregnancy: a cohort study

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Introduction: Under 'Option B+' many prevention of mother-to-child HIV transmission programmes in Africa initiate pregnant women on lifelong antiretroviral therapy (ART) at their first antenatal clinic (ANC) visit. However concerns have been raised regarding patient readiness before ART initiation and whether immediate ART initiation in pregnancy may contribute to increased non-adherence.

Materials & Methods: As part of a larger study of ART use in pregnancy, we enrolled into a prospective cohort consecutive ART-eligible pregnant women making their first ANC visit at a primary care facility in Cape Town, South Africa, between April 2013 and June 2014. Before July 2013, eligibility was based on CD4 cell count ≤350 cells/μl ('Option A'), usually with a 1-2 week delay from the first ANC visit to ART initiation; thereafter all women were eligible regardless of CD4 cell count ('Option B+') and typically started ART on the same day as first ANC visit. All women received standardized counselling before starting a fixed-dose regimen. Study interviews were conducted separately from the ART service through one week postpartum and included self-reported adherence based on 30-day recall.

Results: In 618 consecutive ART-eligible women (median age, 28 years; median gestation, 21 weeks; 54% newly diagnosed with HIV), more than two-thirds of women (71%) started ART immediately; this proportion was higher under 'Option B+' versus 'Option A' (p<0.001). 15% percent of women reported at least one missed ART dose. Missed doses were reported more frequently among younger women (p=0.022) and women diagnosed with HIV before the current pregnancy (p=0.015). In women initiating ART immediately, 15.2% reported a missed dose during pregnancy, compared to 14.7% of women who did not start ART at the first ANC visit (risk ratio, 1.01; 95% CI:0.88-1.15; p=0.883). This finding did not vary after adjustment for demographic and clinical measures, and was consistent when restricted to women with CD4 cell counts ≤350 cells/μl.

Conclusions: These results suggest that same-day ART initiation in pregnant women is not associated with reported missed ART doses during the antenatal period. While these results are reassuring for ART programmes implementing 'Option B+', further research is required to examine adherence in care over time, particularly postpartum.

No conflict of interest
Abstract: 93

Prevention of Mother-to-Child transmission

National estimates of mother-to-child transmission of HIV-1 at 6 weeks and 9 months in Kenya

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Background: To reach targets for elimination of perinatal HIV infection, Kenya has expanded prevention of mother-to-child transmission of HIV (PMTCT) coverage. We evaluated PMTCT program effectiveness and factors influencing MTCT in a nationwide survey.

Materials & Methods: We conducted probability-proportional-to-size sampling of 120 clinics in Kenya from July-December 2013. Staff surveyed mother-infant pairs attending 6-week and 9-month immunizations, offered HIV retesting to HIV-uninfected mothers, and collected blood spots from infants of HIV-infected mothers for HIV DNA testing. Transmission risk (TR) was calculated by dividing number of DNA-positive infants by infants at risk at each time point. Multivariable regression models weighted for survey design and clinic-level clustering compared exposures between HIV-infected and uninfected infants.

Results: Among 2521 mother-infant pairs surveyed, 1502 attended 6-week and 1019 attended 9-month visits. Overall, 2423 (94.7%) reported HIV test in pregnancy or prior HIV diagnosis, of whom 200 (7.4%) were HIV-infected, 86 (40.7%) diagnosed in pregnancy. Of 200 infants born to mothers with known HIV, 188 underwent HIV-testing, of whom 7.2% (95% CI: 3.7-13.5%) were HIV-infected. HIV-TR was 8.8% (CI: 4.0-18.3%) in the 6-week cohort and 4.8% (CI: 1.3-15.6%) in the 9-month cohort. Including mothers with incident HIV since pregnancy, 9-month postpartum HIV-TR was 8.7% (3.1-22.0%). Mothers of HIV-infected infants were less likely to know their CD4 count (18.6% vs 58.5%, p=0.02) or disclosed their status to male partners (24.5% vs 80.6%, p<0.001) than mothers of uninfected infants. Infected infants were more likely to be female (82.3% vs 17.8%, p=0.03). Overall, 69% of HIV-infected mothers received antiretroviral drugs (ARVs) during pregnancy, 65% at delivery, 64% postpartum; 93% of infants. HIV-TR was higher in mothers reporting no ARVs compared to mothers receiving ARVs during pregnancy (aOR=6.4; CI: 1.2-34.4), at delivery (aOR=10.9; CI: 1.9-62.4), or postpartum (aOR=6.7; CI: 1.2-37.4). Infant ARVs were associated with lower TR (aOR=0.1; 0.01-0.4).

Conclusions: MTCT was appreciable despite high coverage of pregnancy HIV testing, likely due to incomplete ARV coverage. Evaluation at 6-weeks and 9-months postpartum yielded differences in TR estimates potentially due to loss and mortality; precision of estimates was limited by sample size. Efforts to improve maternal and infant ARV use remain critical to attain PMTCT goals.

No conflict of interest

Abstract: 94

Prevention of Mother-to-Child transmission

Lymphocyte subsets among HIV-exposed uninfected infants from birth to 12 months of age in IMPAACT P1025 study: Protective role for B cells?

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Background: The role of infant B cells and their immunoglobulin products in preventing perinatal HIV transmission has not been fully explored. There is evidence of a protective effect of infant B cells and immunoglobulins when comparing 5-year HIV survivors to non-survivors. Whether or not B cell proliferation may have a protective effect in perinatal HIV is a critical area of HIV pathogenesis to understand. HIV-exposed but uninfected (HEU) infants are exposed during intrauterine life to HIV and its antigens which may penetrate the placental barrier and potentially lead to infant immunologic activation. We hypothesized that lymphocyte subsets are altered in HEU compared to HIV-unexposed healthy (HUU) infants.

Materials & Methods: We compared CD4, CD8, CD4/CD8 ratio and CD19 B cell counts (relative and absolute) between HEU infants enrolled in the International Maternal Pediatric Adolescent AIDS Clinical Trials Group (IMPAACT) protocol 1025 and HUU infants enrolled in the Pediatric AIDS Clinical Trials Group (PACTG) protocol 1009. Lymphocyte subsets were measured from birth to 12 months of age. Infants were divided into 3 age groups: 0-3, 3-6 and 6-12 months of age. A multivariable general linear model was used, for each age group, to estimate the association between HIV exposure status and each of the lymphocyte subset measurements adjusting for age, sex and race/ethnicity.

Results: A total of 1338 HEU and 285 HUU infants were included in this analysis. HEU infants at 6-12 months of age had higher absolute CD4 counts than HUU infants and the difference remained significant after adjusting for age, sex and race/ethnicity (adjusted mean: 3236 vs. 2909 cells/mm$^3$, p = 0.02). HEU infants in the 3-6 and 6-12 month age groups had lower CD8% as compared to HUU infants; the difference remained significant only for the 3-6 month age group in adjusted analysis (adjusted mean: 16% vs. 17%, p = 0.02). The CD4/CD8 ratio was higher for HEU infants at 3-6 months of age, compared to HUU infants (adjusted mean: 3.2 vs. 2.9, p = 0.04). HEU infants at 3-6 and 6-12 months of age also had higher absolute and percentage of CD19 B cell counts than HUU infants (adjusted mean: [3-6 months: 2114.7 vs. 1671.0 cells/mm$^3$, p = 0.002; 29.6% vs. 25.3%, p < 0.001]; [6-12 months: 2156.2 vs. 1511.2 cells/mm$^3$, p < 0.001; 29.2% vs. 24.4%, p < 0.001]). There were no significant differences in CD4% and absolute CD8 counts between HEU vs. HUU infants, across all of the 3 age groups.

Conclusions: Lymphocyte subsets among HEU infants differed from those of HUU infants, but there was no evidence of significant immune deficiency. HEU infants at 3-6 and 6-12 months of age had significantly higher CD19 B cell counts (absolute and relative) than HUU infants, which may account for the higher immunoglobulin levels reported in HEU children. Increased CD19 B cells may be the consequence of intrauterine exposure to HIV viral antigens and/or maternal immune activation. B cells could possibly play a protective role in prevention of perinatal HIV transmission and requires further research.

No conflict of interest

Abstract: 95

Prevention of Mother-to-Child transmission

Raltegravir for the prevention of mother-to-child transmission of HIV

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Background: Raltegravir (RAL), though currently category C in pregnancy, and not recommended for use in newborns, has been used in exceptional cases for prevention of
mother-to-child-transmission (PMTCT). We report on the outcomes of 14 infants exposed in utero to RAL, and the first newborn to be treated with RAL for 6 weeks for PMTCT.

Materials & Methods: Infants born to mothers treated with RAL during pregnancy at the Centre Maternel et Infantile sur le Sida (CMIS) mother-child cohort between 2010-2014 were included in the study. RAL levels were tested on the first available stored plasma sample after birth, and in the treated newborn, therapeutic drug monitoring was done at weekly intervals.

Results: In RAL-exposed infants, RAL was given to mothers at standard dosing of 400 mg BID, started at a mean GA of 30 weeks (range pre-conception-37.5 weeks). Indications for RAL included drug resistance, and/or detectable viral load in the third trimester. Mean GA was 38.5 weeks (±1.76), and mean birthweight was 3200g (±540). There were no clinical adverse events noted among RAL exposed infants (mean follow up time 119 weeks, range 48-144), and all were confirmed HIV negative. RAL levels tested in two exposed newborns at 16 and 30 hours of life were detectable at 0.9345 mg/L and 0.0381 mg/L, respectively, and undetectable in 6 other infants tested at days 4-14. RAL granules for suspension (Merck, special access) were obtained for the prophylaxis of a term newborn (39 weeks GA) from a mother with multidrug-resistant virus, and started at 1.5 mg/kg BID, along with zidovudine and lamivudine at standard doses. Therapeutic drug monitoring for RAL (peak and trough) were done weekly, and RAL levels were consistently above the targeted trough for treatment (0.02 mg/L) for the 6 week duration of therapy. RAL was well tolerated and at follow-up the infant was confirmed HIV negative.

Conclusions: RAL in late pregnancy had no adverse clinical effects on infants exposed in utero. RAL treatment in the newborn at doses of 1.3-1.6 mg/kg BID resulted in therapeutic drug levels. Given the detectable levels of RAL in the first 30 hours of life in exposed infants, the timing and role of RAL in PMTCT should further be considered.

No conflict of interest
Abstract

£4 weeks of acART before delivery and 0.12% with >4 weeks of acART before delivery. Of two VT cases that occurred despite >4 weeks of acART, one was associated with poor maternal adherence, the other with incomplete virologic suppression despite good adherence. An additional 12 infected infants were identified after 3 months of age. Eight of these 12 mothers were Canadian born (4 white, 4 Aboriginal) and 11/12 delivered in provinces with opt-out antenatal screening programs. On multivariate analysis of all 1996 MIP, receipt of no/£4 weeks versus >4 weeks of acART was significantly associated with earlier year of birth, province/territory of birth and maternal risk acquisition category (28.4% IDU; 11.6% sex; 12.3% other) (all p<0.01).

Conclusions: VT continues to occur in Canada despite a free universal access healthcare system. The observations that 12/45 infected infants were identified after 3 months of age and that 11/12 of those were in provinces with opt-out prenatal screening programs suggest that lack of access to routine prenatal care is a major issue contributing to ongoing VT in Canada.

No conflict of interest

Introduction: HIV exposed uninfected (HEU) infants are at increased risk of adverse health outcomes when compared to unexposed uninfected infants, though the precise cause is yet unknown. Our objective was to study the association between maternal health status at the time of delivery and infant health outcomes.

Material & Methods: HEU infants followed in the CMIS mother-child cohort were eligible for the study. Infants born to mothers with CD4 count <350 cells/mm$^3$ and detectable viral load at time of delivery were matched by year of birth, gender and ethnicity to infants born to mothers with delivery CD4 count >350cells/mm$^3$ and undetectable viral load (n=133). Data on health outcomes was extracted by chart review, and compared among infant groups defined by maternal health status.

Results: There were no significant differences in gestational age, birthweight, APGAR scores, or growth parameters (weight, length and head circumference) at 6 and 12 month of age, or rate of hospitalization in the first two years of life, among infants born to mothers with delivery CD4 count <350 cells/mm$^3$ (n=67) vs. >350cells/mm$^3$ (n=66). There was however a higher rate of infection in the first 6 months of life (0.05/person-week vs. 0.02/person-week, p=0.002). Infants born to mothers with detectable viral load (n=41) had lower birthweight and mean gestational age as compared to infants of mothers with undetectable viral load (n=89) (2914±621g vs. 3201±614g, p=0.01; and 37.9 ±2.83 weeks vs. 38.7 ±2.2 weeks, p=0.055), though there were no differences in their subsequent growth parameters. While there was no difference in the overall rate of infection in the first 6 month of life, there was a significantly higher rate of hospitalization (0.61/person-year vs 0.22/person-year, p=0.001) in the first two years of life among infants born to mothers with detectable vs undetectable viral load.

Conclusions: Maternal CD4 count and viral load at delivery may have an impact on health outcomes among HEU infants, with increased rate of infection seen among infants born to mothers with CD4 count<350, and higher rate of hospitalization seen among infants born to mothers with detectable viremia. Further work needs to be directed at understanding the contributing factors.

No conflict of interest

Abstract: 97

Prevention of Mother-to-Child transmission

Health outcomes among HIV-exposed uninfected infants in Quebec, Canada

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Introduction: HIV exposed uninfected (HEU) infants are at increased risk of adverse health outcomes when compared to unexposed uninfected infants, though the precise cause is yet unknown. Our objective was to study the association between maternal health status at the time of delivery and infant health outcomes.

Material & Methods: HEU infants followed in the CMIS mother-child cohort were eligible for the study. Infants born to mothers with CD4 count <350 cells/mm$^3$ and detectable viral load at time of delivery were matched by year of birth, gender and ethnicity to infants born to mothers with delivery CD4 count >350cells/mm$^3$ and undetectable viral load (n=133). Data on health outcomes was extracted by chart review, and compared among infant groups defined by maternal health status.

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Conclusions: Maternal CD4 count and viral load at delivery may have an impact on health outcomes among HEU infants, with increased rate of infection seen among infants born to mothers with CD4 count<350, and higher rate of hospitalization seen among infants born to mothers with detectable viremia. Further work needs to be directed at understanding the contributing factors.

No conflict of interest
Abstract: 98

Prevention of Mother-to-Child transmission

Eliminating mother-to-child transmission of HIV in the UK: what is left to do?

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Introduction: WHO criteria for the elimination of mother-to-child transmission of HIV (MTCT) include ≤ 50 new paediatric infections per 100,000 live births and a transmission rate of <2% in non-breastfeeding populations. Currently approximately 800,000 women give birth in the UK annually, >95% take up routine antenatal screening, and MTCT in diagnosed women reached an all-time low of 0.6% in 2007-11. However, small numbers of HIV-infected children born in the UK are still reported each year, two-thirds are born to undiagnosed women. The findings of a previous audit of perinatal HIV in English births 2002-2005 were fed into national standards and guidelines. We aimed to review cases of perinatal HIV in children born in the UK in recent years in order to improve our understanding of the timing and circumstances of MTCT in the UK, and inform screening protocols.

Materials & Methods: Children diagnosed with HIV are routinely reported to the National Study of HIV in Pregnancy and Childhood, a prospective surveillance study of pregnancies in all HIV-infected women in the UK and their infants. We identified all cases of perinatal HIV infection in children born in the UK 2006-2013, reported by April 2014. Supplementary maternal and infant data was collected through structured telephone interviews with paediatric, obstetric and/or HIV clinicians for each case.

Results: Approximately 9,200 live births to diagnosed HIV-positive women were reported in the UK 2006-2013, and 108 perinatally infected children born 2006-2013 were reported. 79% of the mothers of these infected children were born in Africa, and only 2% likely acquired HIV through injecting drug use. Although many cases were multifactorial, one main contributing factor was identified in each case. Of the 67 women who were undiagnosed by the time of delivery: 28 women declined antenatal HIV testing; 23 tested negative at antenatal screening and acquired HIV later in pregnancy or postnatally; 4 booked very late for antenatal care and test results were only available after delivery; in 7 cases there was a problem with processing or reporting the HIV test result; and in 5 cases there was minimal information. Of the 41 women diagnosed before delivery: 14 were reported to have difficulty engaging with HIV care and/or adhering to treatment during pregnancy; 9 booked late for antenatal care with short duration of treatment; 7 paediatric infections were probably acquired postnatally through undisclosed breastfeeding; 3 infants were delivered pre-term with short duration of treatment; two women acquired HIV during pregnancy after testing negative; in one case there was a problem with the HIV test or result; in 5 cases none of these factors was identified. 68% of women were reported have experienced at least one complicating issue during the pregnancy, e.g. uncertain immigration status, inadequate housing, mental health problems, incarceration.

Conclusion: The WHO threshold for elimination of paediatric HIV has been reached in the UK on a population level. Nevertheless, investigating the causes and circumstances of the remaining small number of transmissions will help to further strengthen screening and management strategies in order to reduce transmission rates even further.

Conflict of interest: The NSHPC received core funding from Public Health England, with additional funding from the UK National Screening Committee (UK NSC). LB is currently funded by the UK Medical Research Council as a Clinical Training Research Fellow and is in receipt of a BHIVA/Janssen scholarship to attend IAS 2015. P.T. received grants from UK NSC, PENTA Foundation, AbbVie, and IATEC/Kendle, and personal fees from the UK NSC and Nutricia.
Abstract: 99

Prevention of Mother-to-Child transmission

Overview of the elimination mother-to-child transmission of HIV in sub-Saharan: Global Plan era

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Background: In 2011, an initiative known as Global Plan was launched with the vision of laying the foundation for the elimination of new HIV infections among children and keeping their mothers alive by 2015. This review was carried out to provide a comprehensive overview of efforts towards elimination of Mother-to-Child Transmission (eMTCT) of HIV in the twenty-one sub-Saharan African priority countries with respect to the progress, the challenges and the recommendations

Materials & Methods: We performed review of the literature published in the period from 2011 to April 10, 2015. Using three databases: PubMed, Scopus and Web of Science, the literature review pools recent evidences on progresses made, challenges encountered and recommendations made by experts on eMTCT of HIV in sub-Saharan Africa. Data were also obtained from the Joint United Nations Programme on HIV/AIDS 2014 progress report on Global Plan.

Results: 39 research papers were included in this study. Between 2009 and 2013, there was 43% total reduction in the number of new infections among children short of the expected 50% reduction. Only eight countries achieved the 50% reduction of new HIV infections among the age group 0-14 years. The final mother to child transmission rate reduced from 28% to 18%. HIV testing and treatment for pregnant women and infants that were exposed to HIV has improved. The percentage of ART coverage among children aged 0–14 years increased appreciably from 11% to 24% in 2013. Integration of Prevention of Mother-to-Child Transmission (PMTCT) and Maternal, Newborn, and Child Health services, has enhanced the uptake and timely initiation of ART among pregnant women living with HIV. Many countries have adopted the option B+ treatment model. There were challenges such as poor adherence, poor post-natal linkage, low Early Infant Diagnosis coverage, low paediatric ART coverage, delays in testing HIV-exposed infants, delay in initiation of ART for HIV-infected children and high unmet needs for contraceptive services. Recommendations such as identification of key barriers, health system strengthening, strengthening community involvement, international collaboration, wise utilisation of resources to strengthen healthcare delivery services among others were made. Behavioral economics can be incorporated into PMTCT programmes in order to increase uptake and improve retention in HIV care with minimal investment. There is need to translate recent evidence based findings into policy and practice without delay and to integrate of stigma-reduction components into PMTCT and other reproductive health services.

Conclusions: There has been a significant progress but more effort is needed in certain countries else achieving the Global Plan goals will be mirage. The poor performing countries need to double their efforts and engage in extraordinary collaborative efforts. It is also important to sustain the momentum in other well performing priority countries. We expect the findings of this study is expected to inform and guide the planning and decision making mechanisms on prevention/elimination of mother-to-child transmission national programmes. Further research is needed to evaluate the impact of Global Plan post-2015, and to consolidate on the strategies to tackle any uncompleted task.

No conflict of interest
Abstract: 100

Prevention of Mother-to-Child transmission

HIV-free survival at six weeks in a cohort of children born to HIV-positive mothers enrolled in Option B+ in Kigali: The Kabeho Study


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Background: In April 2012, Rwanda began implementing a policy to initiate all HIV-positive pregnant women on lifelong antiretroviral treatment (‘Option B+’). In April 2013, the Elizabeth Glaser Pediatric AIDS Foundation (EGPFAF) and Rwanda’s Ministry of Health began the Kigali Antiretroviral and Breastfeeding Assessment for the Elimination of HIV (Kabeho) Study. The study aims to assess HIV-free survival from birth to 24 months of age among HIV-exposed children with mothers enrolled in Option B+.

Materials & Methods: HIV-positive women were enrolled from their third trimester of pregnancy until two weeks postpartum at 14 Kigali health facilities that serve > 50 HIV-positive pregnant women/year. At enrollment, HIV and ART history, medical care, and laboratory information were collected. Delivery information and birth outcomes were recorded from maternity units as soon as possible after delivery. At 6 weeks of age, PCR for HIV diagnosis was done by the National Reference Laboratory using Roche COBAS Ampliprep/TaqMan HIV-1 qualitative test. Positive results were confirmed on second specimen.

Results: Of the 608 infants born in the cohort, 9 (1.4 %) were still births, 10 (1.6 %) spontaneous preterm deliveries and 7 (1.2 %) infants had birth defects. Of the 572 infants with known birth weight, 33 (5.8 %) had birth weight below 2,500 grams. By six weeks of age, 11 (1.8 %) additional infant deaths occurred and 7 (1.2 %) of them died within the first 24 hours of life. Of the 588 children alive at six weeks, 2 (0.3 %) were confirmed to be HIV-positive. The overall HIV-free survival at 6 weeks was estimated at 96.8% (95% CI: 95%-98%).

Conclusions: Provision of ART to all Kabeho Study women resulted in low mother-to-child HIV transmission (0.3%) before six weeks of age, and mortality in this HIV-exposed cohort is much lower than the 2.7% neonatal mortality rate in the 2010 Rwanda Demographic and Health Survey (DHS).

No conflict of interest

Abstract: 101

Prevention of Mother-to-Child transmission

Systematic review of perinatal HIV transmission from breastfeeding for up to twelve months when the mother has viral suppression with combination antiretroviral therapy


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Abstract  

Background: The reduction of perinatal HIV transmission to <1% when pregnant women are given antiretroviral therapy (ART) in the absence of breastfeeding and birthing complications has been a key breakthrough of modern infectious disease prevention. However, there remains limited comprehensive knowledge of the current risk associated with breastfeeding. We undertook a systematic review to determine the risk of perinatal transmission through breast milk among women on combination ART (cART). Understanding this risk is paramount given the discrepancies in global guidelines, and heightened concerns of breastfeeding in high-income countries among communities where formula feeding may not be acceptable, feasible, affordable, sustainable or safe.

Materials & Methods: We searched electronic databases for relevant observational studies and randomized controlled trials (RCTs) without restriction to date publication, language or study jurisdiction. To increase sensitivity, we reviewed reference lists of identified studies and review articles, and hand-searched selected journals to ascertain recently published articles . Included studies reported cART use among HIV-positive pregnant women prior to delivery with stated viral load responses, who then breastfeed for any length of time with reported perinatal HIV transmission rates to the infants. Two reviewers independently extracted methodological characteristics and outcomes and assessed risk of bias. Meta-analytic techniques calculated rates of HIV transmission among breast-fed infants in included studies.

Results: Of 5270 citations, 10 studies met the eligibility criteria (three RCTs and seven observational studies) of which five were included in the meta-analysis, with a sample size of 2059. The transmission rates were 2.9%, 95%CI [2.2-3.8] at one month; 3.6%, 95%CI [2.7-4.0] at three months; 4.0%, 95%CI [3.1-5.2] at six months; and 5.1%, 95%CI [4.0-6.5] at 12 months. Transmission rates increased by 1.1% in the early perinatal breastfeeding period (1-to-6 months). Late transmissions increased by 1.1% from 6 to 12 months.

Conclusions: Though limited by a predominance of observational studies, our findings suggest an overall attributable HIV transmission risk of at least 2.2% during the early perinatal period with heightened risk during the first year when the mother on cART is breastfeeding for any length of time. This data can facilitate counseling for mothers experiencing difficulty adhering to formula-only guidelines in high-income settings.

No conflict of interest

Abstract: 102

Prevention of Mother-to-Child transmission

Raltegravir (RAL) Pharmacokinetics (PK) and Safety in HIV-1 Exposed Neonates at High Risk of Infection (IMPAACT P1110)


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Background: RAL is primarily metabolized by UGT1A1, whose activity is low at birth and increases exponentially over the first weeks of life. IMPAACT P1097 demonstrated that RAL crossed the placenta well and elimination of transplacentally acquired RAL in infants whose mothers received RAL during pregnancy was highly variable and prolonged. The objectives of IMPAACT P1110 are to evaluate the pharmacokinetics and safety of RAL and to determine an appropriate neonatal dose during the first 6 weeks of life using a two cohort

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adaptive design, where PK data from Cohort 1 are included in PK modeling to guide daily dosing in Cohort 2.

Materials & Methods: IMPAACT P1110 is a Phase I multicenter PK study of RAL in full-term HIV-1 exposed neonates at high risk of acquiring HIV-1 infection. Cohort 1 infants received RAL administered as a single oral 3 mg/kg dose within 48 hours of birth in addition to standard of care antiretrovirals for PMTCT prophylaxis, and a second dose administered at 7-10 days of life. Pharmacokinetic sampling was done around the first dose (pre-dose and 1-2 hours, 4-8 hours, 12 hours, 24 hours post-dose, random sample on day 3-4 of life) and second dose (pre-dose and 1-2 hours, 24 hours post-dose). PK samples were analyzed for RAL concentrations on a rolling basis using a validated HPLC-MS-MS method. Protocol exposure limits for each subject are Cmax ≤ 19.6 µM and AUC12 ≤ 63 µMxhr.

Results: 6 mother-infant pairs enrolled in Cohort 1 (all RAL-unexposed in utero). Complete PK parameters following the first single dose are available for 5 of the 6 neonates. Geometric mean (%CV) half-life was 12.8 hours (19.6%), Cmax 6.9 µM (27.6%), and AUC12 of 60.6 µMxhr (31.5%). Although the Cmax upper limit was not exceeded by any subject, two patients exceeded the AUC12 upper limit. All infants tolerated the two single oral doses well.

Conclusions: Given that 40% (2/5) infants exceeded the AUC12 target, these data suggest that daily neonatal dosing with RAL 3 mg/kg in RAL unexposed infants may be excessive. Dosing with 2 mg/kg for first dose is now under study. Neonates exposed to RAL in utero may require a different dosing strategy and are also being studied in P1110.

Conflict of interest: H Teppler, ML Rizk, and C Welebob are employees of Merck Sharp & Dohme Corp, a subsidiary of Merck & Co, Inc, and may own stock and/or stock options in the company. All other authors report no potential conflicts.
PK model was developed incorporating these data with RAL concentration data from 24 infants and children ages 4 weeks to < 2 years enrolled in IMPAACT P1066, a phase 1/2 study of RAL in HIV infected infants and children. Population modeling using PsN/3.7.6, NONMEM/7.3.0 and R/3.1.0 was performed to estimate typical PK parameters, which were then used in simulations of potential dosing regimens. The regimen that best met PK exposure targets (Cmax, Cmin, AUC) defined for safety and efficacy from studies in older infants, children, and adults was selected for future evaluation in a second cohort of neonates.

**Results:** A 2-compartment model with first order absorption provided best fit. Apparent clearance changed dramatically from very low at birth to fully mature at 6 months. The absorption rate also changed rapidly, from 16% at birth to 90% of the maximum rate within 2 weeks. Despite the considerable maturation and body-size changes, the model described the observed RAL concentration data well. Simulations suggested that a regimen of 1.5 mg/kg once a day from birth through day 7, followed by 3 mg/kg twice daily until 4 weeks of age, then 6 mg/kg twice daily to age 6 weeks would best meet the PK exposure targets and was selected as the initial regimen to be studied in a second cohort.

**Conclusions:** There are few antiretrovirals with an appropriate formulation and adequate PK data for use in neonates. By combining RAL concentration data from a small group of neonates receiving only 2 RAL doses with that from older infants and children receiving daily dosing, we were able to develop a population PK model and perform simulations that allowed us to select a developmentally appropriate RAL daily dosing regimen for evaluation in Cohort 2 of P1110.

*Conflict of interest: H Teppler, M Rizk, L Wenning, and A Chain are employees of Merck Sharp & Dohme Corp, a subsidiary of Merck & Co, Inc, and may own stock and/or stock options in the company. All other authors report no potential conflicts.*
7th International Workshop on HIV Pediatrics

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Abstract Book Only
Abstract

Prevention of Mother-to-Child transmission

No evidence that maternal immune compromise is associated with infectious morbidity in South African HIV exposed uninfected infants of mothers on maternally indicated cART


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Background: Southern African studies in the pre-antiretroviral therapy era observed an association between low maternal CD4 count and HIV exposed uninfected (HEU) infant morbidity. In the era of expanded access to combination antiretroviral therapy (cART), do HEU infants born to mothers on maternally indicated cART with current or prior immune compromise still experience greater infectious morbidity than those of mothers not immune compromised receiving simpler vertical transmission prophylaxis (VTP)?

Materials & Methods: A prospective cohort study from 2012-2014 identified HIV-infected and HIV-uninfected mothers and their newborns from a single community midwife unit. HIV-infected women received maternally indicated cART for CD4 count <350 cells/mm$^3$ or WHO stage 3/4, otherwise zidovudine monotherapy was received for VTP. The primary outcome, at least one infectious cause hospitalization or death before 6 months of age, was determined using the province-wide electronic hospital administration system allowing complete outcome ascertainment. Odds ratios (OR) for the primary outcome in infants born to mothers on cART compared to infants born to mothers on VTP were calculated by multivariable logistic regression.

Results: Of 89 HIV-infected mothers and their HEU infants, 47 (53%) mothers received maternally indicated cART and 42 (47%) received VTP. An infectious cause hospitalization occurred in 8 (17%) infants born to mothers on cART and 7 (17%) infants born to mothers on VTP, there were no deaths. The unadjusted OR for at least one infectious cause hospitalization was 1.03 (95% CI 0.33,3.20) for cART infants relative to VTP infants. After controlling for maternal age, timing of HIV diagnosis, maternal HIV viral load or any breastfeeding at 2 weeks or 6 months, there remained no difference.

cART mothers were significantly older (median 29.2 years (IQR 26.2,32.4) vs. 27.4 (IQR 23.4,30.4), p=0.04) and more often diagnosed with HIV pre-pregnancy (33/47 (70%) vs. 14/42 (33%), p=0.001). Median antenatal and delivery CD4 counts were significantly lower in cART than VTP mothers (antenatal: 332 cells/mm$^3$ (IQR 232,420) vs. 571 (IQR 428,623), p=0.01; delivery: 313 cells/mm$^3$ (IQR 214,459) vs. 423 (IQR 288,556), p=0.02). The median CD4 count increased from antenatal to delivery in cART mothers by 17 cells/mm$^3$ (IQR -115,143) compared to a median decrease in VTP mothers of 109 cells/mm$^3$ (IQR -238,30) (p<0.01). Maternal delivery HIV viral load was <40 and >1000 copies/ml in 30 (64%) and 5 (11%) cART mothers and 1 (2%) and 21 (50%) VTP mothers respectively (p<0.01). Infant gestational age, birth weight, immunizations and co-trimoxazole prophylaxis did not differ. Most infants were never breastfed (56/89 (63%)). Median maternal antenatal and delivery CD4 count were no different between outcome groups (antenatal: 467 cells/mm$^3$ (IQR 349,642) vs. 411 (IQR 285,521), p=0.23; delivery: 308 cells/mm$^3$ (IQR 218,601) vs. 350 (IQR 249,487), p=0.96) and neither did the change in CD4 count nor the HIV viral load differ.

Conclusion: There is no evidence that HEU infants of mothers on maternally indicated cART experience greater infectious morbidity to infants of mothers not severely immune compromised. Maternal CD4 count dynamics and delivery HIV viral load were not associated with infant infectious morbidity.

No conflict of interest
Abstract: 105

Prevention of Mother-to-Child transmission

Health facility challenges to the provision of Option B+ in Kenya

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Background: Current World Health Organization guidance recommends lifelong antiretroviral therapy (ART) for all pregnant and breastfeeding women (Option B+) in settings with generalized HIV epidemics. We explored provider perspectives on potential barriers and facilitators in the provision of Option B+ in Kenya.

Materials & Methods: We conducted four focus groups with 30 health care providers between September and November 2014 to explore challenges that health facilities are facing in implementation of Option B+, which has recently been rolled out in western Kenya. Transcripts were coded using the Dedoose software; based on the literature, topics from interview guides, and emerging themes from transcripts. Excerpts from broad codes were then fine-coded using an inductive approach.

Results: Major themes that emerged included a preference for Option B+ over prophylactic regimens, with the major advantage cited being elimination of CD4 count testing as requirement for treatment initiation. Shortage of drugs and staff, and the practice of same-day initiation into treatment were challenges raised. Providers expressed concern that pregnant women have little time to accept and disclose their HIV status when they are immediately initiated on treatment; which could potentially lead to stigma, conflict, or violence in the home. An additional challenge noted was the possibility of women disengaging from care if their child tests HIV-negative at 18 months and they no longer feel the need to adhere to treatment to protect their child. Suggested facilitators for long-term retention and adherence included strategies for individual clients (continuous adherence counseling, tracing of clients who are lost-to-follow-up, and text messages), couple/group strategies (couple testing, assisted disclosure, treatment buddies, and support groups), community strategies (reducing stigma, community mentor mothers), and changes in service provision (integration of ART with other services and longer clinic hours of operation).

Conclusions: This study highlights important challenges at the health facility level related to Option B+ roll-out in western Kenya. Adaptation of identified facilitators may increase linkage, retention and adherence to life-long treatment for pregnant women in Kenya, contribute towards elimination of mother-to-child HIV transmission, and improve maternal and child outcomes.

No conflict of interest

Abstract: 106

Prevention of Mother-to-Child transmission

Using Text Messaging to maximize adherence and retention for women and infants in the context of Option B+ in Kenya

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Background: Key challenges in the provision of lifelong anti-retroviral therapy (ART) to pregnant and breastfeeding women (Option B+) include achieving long term ART adherence and retention in care. Evidence suggests these challenges may be addressed using mobile text messaging. However, the efficacy and acceptability of this intervention in context of Option B+ has yet to be ascertained. We evaluated the acceptability of mobile text messaging as a means of supporting women's long term ART adherence and retention in care as Option B+ is being rolled out in Kenya.

Materials & Methods: Forty in-depth interviews with 20 HIV-positive pregnant/postpartum women and 20 male partners, as well as 4 focus groups with 30 health workers, were conducted during the period September-November 2014 in rural Nyanza, Kenya. Transcripts were coded using the Dedoose software program based on the literature, topics from the interview guides, and emerging themes from the transcripts. Excerpts from broad codes were then fine-coded using a grounded approach.

Results: Themes that emerged in the data included overall acceptability, preferred content of messages, message sharing and potential risks of receiving HIV-related text messages. The overall acceptability of a patient-tailored mobile text messaging intervention was evident among most participants. They anticipated that the messages would provide useful and educational information, and proposed the content of messages include specific reminders for clinic visits and infant immunizations. In addition, participants recommended that messages encourage HIV testing for infants and HIV-negative partners, as well as promote ‘positive living’ with HIV. Because mobile phone sharing was common, participants reported potential risks of inadvertent disclosure of HIV status. All participants emphasized the need to keep messages confidential. They suggested that disclosure between couples be required if partners received messages. To further reduce risk of involuntary disclosure, many participants preferred text messages be kept generic and omit any specific mention of HIV.

Conclusions: Overall, mobile text messaging was viewed as an acceptable intervention for promotion of long-term ART adherence and retention in HIV care among pregnant women. The findings are being used to refine a text messaging intervention for pregnant/postpartum women and male partners at sites rolling out Option B+ in Kenya.

No conflict of interest

Abstract: 107

Prevention of Mother-to-Child transmission

Enhanced Neonatal Prophylaxis Regimens in High-Risk and Breastfed Infants as compared with current recommendations

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Background: An estimated 240,000 children are infected with HIV each year, with the primary method of infection being mother-to-child transmission. The risk of vertical transmission can be dramatically reduced through maternal HAART and infant ARV prophylaxis. Current WHO recommendations advise four to six weeks of nevirapine or zidovudine given to the infant as post-exposure prophylaxis. A systematic review was undertaken to determine if there is evidence to advise enhanced prophylaxis regimens in certain high-risk or breastfed infants.

Materials & Methods: By searching Cochrane CENTRAL, EMBASE, PubMed databases from 2005-2015, as well as CROI and IAS abstracts, relevant studies were identified. Randomized controlled trials and cohort studies examining the use of combination or prolonged infant regimens in HIV-exposed infants were included. The search returned 1185 studies, which were screened by title and abstract by two independent reviewers. Following the initial screening, 45 full-text articles were examined in further detail.
Results: Four studies were ultimately eligible and included in this review. Three studies examined multi-drug prophylaxis regimens in formula-fed, high-risk, HIV exposed infants. Of these three, two were cohort studies and one was a randomized controlled trial. The randomized controlled trial showed reduction in intrapartum transmission rates with two-drug and three-drug combination regimens, as compared to a mono-drug regimen. No significant difference in efficacy was shown between the two and three-drug regimens, although, the three drug regimen had more adverse events. A prospective cohort study comparing mono-drug prophylaxis with a three-drug regimen showed significantly lower rates of transmission in the cohort of infants receiving combination prophylaxis. Only one randomized controlled trial examining prolonged ARV prophylaxis in a breastfed population was identified. In this study, six months of nevirapine resulted in lower HIV transmission rates as compared to the standard six-week nevirapine regimen. Of the four trials, only two included mothers on HAART, which is the current standard of care in pregnancy. 

Conclusions: Although data on this topic is limited, available evidence does suggest that using combination ARV regimens in high-risk infants reduces intrapartum transmission, and that using prolonged mono-drug prophylaxis in breastfed infants results in lower transmission rates. However, the additional benefit of prolonged regimens in the context of HAART remains unclear. More research is needed in this area to further inform recommendations, regarding which specific ARVs should be included in combination regimens, as well as the optimal duration of regimens. Considerations regarding resistance, toxicity, and feasibility must also factor into future recommendations. Furthermore, as more pregnant women initiate HAART as a result of expanding PMTCT programs and adoption of Option B+, further research on the utility of infant prophylaxis in the context of maternal HAART is needed.

No conflict of interest

Abstract: 108

Implementation research on PMTCT and pediatric treatment programs

Geographic origin trends among HIV+ mothers and children in Canada and impact on vertical HIV transmission rates

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Background: Migration contributes significantly to new HIV cases in Canada. This study describes geographic origin trends among HIV+ mothers and perinatally infected children and impact on vertical HIV transmission (VT) rates among HIV+ mother-infant pairs (MIP) in Canada from 1990-2013.

Materials & Methods: The Canadian Perinatal HIV Surveillance Program collects data at 22 centres. The primary focus is on MIP with an infant born in Canada and identified prior to/within 3 months of birth; MIP with Canadian-born infants identified after 3 months, and HIV+ children born abroad are also tracked. Data reviewed for this study included: maternal country of origin, clinical characteristics, antiretroviral usage and infant outcome. Logistic regression determined VT rate differences for foreign-born (FBM) versus Canadian-born mothers (CBM).

Results: Among 3877 MIP, 2089 (53.9%) mothers were FBM. Of 1481 (70.9%) African mothers, 30.7%, 20.1%, 17.7%, and 16.7% came from East, Central, Horn, and West Africa, respectively. CBM accounted for 66.7% (971/1456) in Western/Central Canada, whereas FBM predominated in Ontario (945/1357, 69.6%; greatest proportion East African, 25.0%) and Quebec (713/1020, 69.9%; greatest proportion Caribbean, 36.2%). The largest numbers of FBM originated from Haiti (12.5%), Ethiopia (8.7%), Congo (7.0%),

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Zimbabwe (5.4%), and Nigeria (4.6%). In the pre-cART era (1990-1996), Haiti contributed 29.9% (90/301) of FBM, decreasing to 13.0% (119/918) in 1997-2007, and 6.6% (52/782) in 2008-2013. Since 2008, Ethiopia (80/782, 10.2%), Congo (64/782, 8.2%), and Nigeria (62/782, 7.9%) predominated. VT rate among Canadian-born children from 1990-2013 was 3.8% (3.0% among FBM) and 1.2% from 2008-2013 (0.7% among FBM). African mothers had lower risk of VT (1990-2013: OR = 0.45, 95%CI 0.29-0.71; 2008-2013: OR 0.35, 95%CI 0.12-1.08) compared to CBM; no differences were seen for other regions. Of 353 HIV+ children (born in Canada or abroad) with FBM, the greatest numbers came from Haiti (48, 13.6%), Ethiopia (33, 9.3%), Burundi (30, 8.5%), and Congo (15, 4.2%).

Conclusions: Geographic origins of HIV+ FBM in Canada have changed over time, shifting from predominantly Haitian in the pre-cART era to predominantly African more recently. African mothers have lower VT rates than CBM. Understanding country-specific cultural and obstetrical/pediatric health issues is imperative to providing optimal care.

No conflict of interest

Abstract: 109

Comprehensive Pediatric HIV care

Effect of promotion on adequate dietary intake and exercise in HIV-infected children

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Introduction: Perinatally HIV-infected children are smaller and shorter than healthy children which caused by various factors including inadequate dietary intake and exercise. There are limited data of effect of the promotion of appropriate diet and exercise in HIV-infected children.

Materials & Methods: Perinatally HIV-infected Thai children aged 12-20 years were enrolled. All children were asked to complete questionnaires (score 0 to 25) about knowledge and attitude on the topic of healthy lifestyle at baseline and after participated in the interactive 1-day camp containing four sessions of 1) Thai nutrition flag, 2) understand nutrition label, 3) selection of food for adequate energy and calcium intake, and 4) having adequate exercise. Children recorded their 3-days diet diary at baseline, month 1, 3, and 6. A trained nutritionist transformed data from this diary to amount of energy and calcium intake per day by using INMUCAL-Nutrients V.3 program, Institute of Nutrition, Mahidol University. Adequate calorie intake per day for boy was defined as ≥2,100 kcal/day and for girl was ≥1,800 kcal/day. The International Physical Activity Questionnaire-Short form (IPAQ-SF) was completed at baseline, month 1, 3, and 6. Fasting total cholesterol and triglyceride were performed at month 0 and 6.

Results: Fifty-eight HIV-infected children, 48% female, median (IQR) age 15.3 (14-16.7) years, weight 41.3 (36.6-47) kg, height 154 (148-160) cm, were enrolled. Median z-score weight-for-age was -1.21 (-1.68 to -0.34) and weight-for-height was -0.41 (-1.07 to 0.46). Fifty-seven (98%) children were on antiretroviral therapy. Median CD4 count was 704 cells/mm3 and 81% had plasma HIV-RNA <50 copies/ml. Median (IQR) knowledge score for pre-test and post-test were 13.5 and 14.5 (p=0.01). There was no difference of attitude about importance of having breakfast regularly, to select variety of food, and having vegetables and fruit between pre-test and post-test (all p>0.4). The attitude of having regular exercise 3-5 times/week between pre-test and post-test were 35% vs. 56% (p=0.004). Median calorie intake at month 0 vs.6 were 1220 vs. 1038 kcal/day (p=0.03). Proportion of children having adequate dietary intake per day at month 0 vs 6 were 6.4% vs. 4.2% (p=0.6). Median calcium intake at month 0 vs. 6 was 360 vs. 318 mg/day (p=0.15). None of the children had adequate calcium intake at baseline.

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Comprehensive Pediatric HIV care

Paediatric HIV diagnosis in non-PMTCT settings: a systematic review

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Background: Less than half of children with HIV are diagnosed and many of these may not present to care via PMTCT. To reach these children, testing in non-PMTCT settings must be considered. We conducted a systematic review investigating paediatric HIV case finding in low- and middle-income countries in four settings: paediatric inpatient, paediatric outpatient, essential programmes for immunisation and nutrition centres.

Materials & Methods: Using an a priori protocol, a search was conducted in PubMed, EMBASE, MSF, Cochrane, Web of Science and Lilacs. The primary outcome was HIV prevalence and secondary outcomes were 1) caregiver acceptance rates, 2) healthcare worker uptake and 3) retention in care at each stage of the cascade. Studies reporting on paediatric HIV prevalence in any of the four settings and published between January 2004 and September 2014 were included. Titles, abstracts and full text were screened and data extracted in duplicate. Authors of eligible included studies were contacted for age-disaggregated data where necessary. Analysis of primary outcomes were disaggregated according to age (0 to 5 years, 5 to 12 years) and the results for children under 5 will be presented here.

Results: 2890 studies were identified with 38 studies reporting primary outcomes included, of which 21 reported secondary outcomes. The majority of studies were conducted in sub-Saharan Africa (n=34). Paediatric inpatient was the most common setting (n=26) followed by paediatric outpatient (n=6), nutrition centres (n=4), and essential programme for immunisation (n=3).

Using random effects analysis we found mean HIV prevalence for children under 5 years was 19.0% (16.0-22.0; 95%CI). For children under 5 years we found mean prevalence rates for each setting: 26.7% (20.3-33.1%; 95%CI) in paediatric inpatients; 5.4% (1.2-9.6%; 95% CI) in paediatric outpatients; 13.2% (2.0-24.3%; 95% CI) in nutrition centres and 4.9% (0.3-9.6%; 95% CI) in essential programme for immunisation.

Mean acceptance by caregivers (n=13) was 90.90% (range 48.50-100%). Five studies reported retention in care outcomes, including a mean of 80.1% of patients receiving test results (n=3), 81.2% of patients in a nutrition centre were referred for HIV care (n=1) and 68.3% enrolment into outpatient HIV care from paediatric inpatient services (n=1).
Conclusions: This systematic review reveals high rates of paediatric HIV prevalence in non-PMTCT settings, in particular in paediatric inpatient and nutrition centres in sub-Saharan Africa. In comparison with background PMTCT programme detection of paediatric HIV of 2% in well-functioning programmes and 5% in poorly functioning programmes, universal testing in paediatric inpatient and nutrition centres would be high yield to identify HIV-positive children and should be included as a focus for national health systems and HIV programs in sub-Saharan Africa. While acceptance of testing by caregivers in these settings is high, more needs to be done to ensure linkage to care.

No conflict of interest

Abstract: 111

ARV Treatment of pediatric HIV infection

Missed opportunities of inclusion and baseline characteristics of HIV-infected children in an early antiretroviral treatment cohort before two years, in West Africa

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Background: The WHO 2010 guidelines recommended to treat all HIV-infected children < two years old. We aimed to describe the inclusion process and its associated factors in a cohort of early antiretroviral therapy (EART) initiated in HIV-infected children < two years old in Abidjan, Côte d’Ivoire and Ouagadougou, Burkina Faso.

Materials & Methods: We included all HIV-1 infected children screened by Dried Blood Spot, < two years old, and whose parents agreed to participate in the MONOD ANRS 12206 project in a prospective cohort to receive an EART based on Lopinavir/r. We used logistic regression to identify the factors associated with inclusion in the cohort.

Results: Among 217 children screened and referred to MONOD health centers, 161 (74%) were included and initiated on EART. The main reasons of non-inclusion (N=56) were fear/denial of the father (27/56; 48%), early mortality (13/56; 24%), HIV-infection controlled negative (9/56; 16%), and ineligibility for geographical/biological reasons (7/56; 12%). The disclosure of the child’s or mother’s HIV status to the father was predictor of EART initiation (adjusted odds ratio (aOR): 3.20, 95% confidence interval (IC95%): 1.55-6.69), as well as being older than 12 months (aOR: 2.05; 95% CI: 1.02-4.12). At EART initiation, the median age was 13.5 months, 70% reached WHO stage 3/4, and 57% had a severe immune deficiency.

Conclusions: Early mortality and fear of father stigmatization were the major reasons of missed opportunities of EART initiation. There is an urgent need to early diagnose infants and early involve fathers in the care of their HIV-infected children, which might improve their future access to EART and health.

No conflict of interest
Abstract: 112

HIV infection and adolescents

Adolescents are at higher risk of attrition from HIV care: results from a cohort study in Ethiopia

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Background: Attrition from HIV care is a huge challenge in all age groups. However, studies describing attrition rates among adolescents are scarce. Since many children living with HIV are now growing to adolescence and adulthood, it is important to understand the challenges of retention in this age group in order to design appropriate interventions. The objective of this study was to compare the rate of attrition from HIV care between adolescents and younger children treated and followed at public health facilities in Ethiopia.

Materials & Methods: We conducted a retrospective cohort study in seven hospitals and one health center in two regions of Ethiopia between April-November 2014. The study population constituted adolescents (age 10-19 years) and children (0-9 years) enrolled in chronic HIV care from January 1, 2005 through December 31, 2013. Trained nurses assisted by site data clerks and under supervision of pediatricians did retrospective chart review using pre-tested data abstraction form. The primary end point was attrition from care (pre or post-ART) defined as occurrence of one or more of the following: death, loss to follow up, and transfer out. We used Cox regression analysis and calculated adjusted hazard ratios (aHR) after controlling for gender, disease stage, CD4, and hemoglobin.

Results: We included 2058 patients (1072 adolescents and 986 children) in the study, and they contributed 2422 person-years of observation (PYO) during pre-ART follow up. Their median age was 10 years and 54% were girls. Being adolescent was the only independent predictor of pre-ART attrition after controlling for covariates [aHR (95% CI)=1.62 (1.25-2.09); p< 0.001]. At the end of the pre-ART follow up, 74.4% were put on ART and they contributed 5984 PYO. Of 1531 put on ART, 93 died during follow up, making the mortality rate 15.5 per 1000 PYO (23.2 versus 8.6 in adolescents and children respectively). Adolescents were at significantly higher risk of attrition from ART follow-up [aHR (95% CI)=2.14 (1.71-2.69); p< 0.001]. Gender was not associated with attrition from care.

Conclusion: Adolescents experienced significantly higher rates of attrition from care both before and after initiation of ART in public health facilities in Ethiopia. Further studies and adolescent-specific interventions are urgently needed.

Conflict of interest: The study was funded through CIPHER grant which was supported by ViiV Healthcare

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HIV infection and adolescents

A View on Pregnancy among HIV Perinatally Infected Adolescents

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Background: Since 1985 our medical team at Instituto de Infectologia Emilio Ribas, São Paulo, Brazil, has been following more than 1,000 HIV-infected children. Currently 400 HIV-perinatally infected children and adolescents are being followed by a multidisciplinary health team, receiving not only antiretroviral therapy and medical assistance, but also information regarding taking care of their own health, family planning and safe sex. The objective of this study was to review the episodes of pregnancies among the adolescent girls and the social and behavioral circumstances of each pregnancy.
**Materials & Methods:** Medical charts from the adolescents who became pregnant were reviewed.

**Results:** Thirty adolescents became pregnant (13 to 24 years old, mean 18.1 years), with 40 pregnancy and 37 live born children. Only 46.2% admitted that the pregnancy was desired. In 80.6% of the cases the sexual partner was aware of her HIV status and only 1 was HIV+. Ninety point six percent had adequate prenatal care (6.1 medical visits during pregnancy), 8.8% were submitted to vaginal labor, 91.2% to C-section and 5 underwent to miscarriage. Nine girls presented more than one pregnancy, 4 with 3 pregnancy and 5 with 2 pregnancy and two had twin births. The mean CD4 near delivery was 513.16 cells/µl and the viral load was less them 1000 copies/ml in 51.6%. Only one child born to this population showed to be HIV-infected, whose mother was drug addicted and abandoned follow up during pregnancy.

**Conclusion:** Untimely and undesired pregnancy may cause negative impact to HIV-infected adolescents and young adults and can bring more difficulties to the ample development of the newborn. Adolescents with PNA HIV infection are becoming sexually active and need innovative interventions programs including procreational choices.

No conflict of interest

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**Abstract:** 114

Comprehensive Pediatric HIV care

12-month costs of care of HIV-infected children initiating early antiretroviral therapy < 2 years in Abidjan, Cote d'Ivoire. The MONOD ANRS 12206 project

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**Background:** To determine the healthcare resource use and costs attributable to the care of HIV-infected infants on early antiretroviral therapy (EART) initiated < 2 years old.

**Materials & Methods:** We assessed the direct costs of care for all HIV-1 infected children <2 years old, whose parents agreed to participate, without tuberculosis, included in an initial prospective cohort to receive an EART based on LPV/r in Abidjan. During the first 12-month on EART, we documented all severe morbid events (SME), leading to death or hospitalization and recorded drug prescriptions, ART and cotrimoxazole prophylaxis delivery, medical exams and consultations with specialists, hospital admissions and routine biological follow-up.

**Results:** We included 99 children, at a median age of 13.5 months (IQR: 6.8 – 18.6); 45% had reached WHO stage 3 or 4 at enrolment. Of these children, 5 (5%) died and 3 (3%) were lost to follow-up. During the first 12 months, 27 children presented 35 SME; the incidence rate was 36.77 per 100 child-years (IC95%: [35.55 – 37.99]). The mean cost of care per child-month reached 672.44 USD. Most of these expenses are borne by the Ivorian national AIDS program: ART (621.47 USD per child-month), cotrimoxazole prophylaxis (31.02 USD per child-month) and routine biological follow-up (6.24 USD per child-month). The additional healthcare resource use costs were 13.71 USD per child-month: 7.27 USD and 6.24 USD for drug prescriptions and medical exams, respectively. This mean cost of healthcare resource use per child-month was lower in children without SME compared to those who had (11.56 USD versus 18.66 USD). The mean cost of care per child-month of a SME was estimated 14.03 USD (IC95%: 9.45-18.60) in children who deceased and 8.03 USD in children who survived.

**Conclusion:** Despite EART based on LPV/r, severe morbidity still occurs and represents a significant healthcare burden. The additional healthcare resource use costs, borne by patient families, remains substantial. In this resource-limited setting, it is crucial to include HIV-
Abstract

Prevention of Mother-to-Child transmission

Breastfeeding did not have negative impact on body mass index of HIV-infected mothers in 4 African countries

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Background: In socio-economic deprived settings breastfeeding is a key survival strategy to infants born to HIV-infected women. HIV-infection is known to cause wasting in people infected. Breastfeeding further increases energy demands. Our objective was to explore the impact of breastfeeding on changes in Body Mass Index (BMI).

Materials & Methods: The data were collected in the ANRS 12174 trial (clinical trial no NCT00640263) in Burkina Faso, South Africa, Uganda and Zambia. We ran a linear mixed model with BMI as the dependent variable and exclusive and predominant breastfeeding (EPBF) duration as the key explanatory variable.

Results: Among 1225 participants, 97% initiated BF in the first week of infant's life for a mean duration of 5.9 (95%CI 5.8- 6.0) and a median of 6.6 months (Interquartile range: 0.9). The mean (standard deviation) age, BMI, CD4 count, and HIV viral load at baseline (day 7) were respectively 27.4 (5.4) years, 24.5 (4.5) kg/m², 579 (198) cells/µl and 39000 (336000) copies/mm³. The hemoglobin concentration (week 14 post-delivery) was 12.1 (1.5) g/dl. For each additional month of EPBF, there was a non-significant decrease in BMI of -0.08 (95% CI: -0.24; 0.08) kg/m² (table 1), and the total mean reduction was -0.50 (95% CI: -1.42; 0.47) kg/m². The mothers’ HIV-1 viral load, disease stage, hemoglobin concentration, the marital and occupational status, breastfeeding initiation time child gender as well as the study treatment arm were not statistically significantly associated with the BMI change. Conversely, the mothers’ age, education level, mode of delivery (vaginal versus C-section) and parity were statistically significantly and positively associated with the BMI change.

Conclusions: According to our findings breastfeeding practice did not have a negative impact in HIV-1 infected mothers’ BMI. EBF should be widely advised for infants born to HIV-infected women in poor resource settings where formula is not safe.

No conflict of interest

Abstract: 116

Comprehensive Pediatric HIV care

Growth and determinants thereof in HIV-infected children on long-term antiretroviral therapy

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Background: Suboptimal growth in HIV-infected children remains of concern despite
good mortality outcomes achievable for children initiated on antiretroviral therapy (ART). The study objective was to describe growth in HIV-infected children on long-term ART and to study social, clinical, immunological and virological factors associated with suboptimal growth.

Materials & Methods: HIV-infected children aged <5 years at ART initiation and with ≥5 years follow-up data were studied at an urban ART site in Gauteng, South Africa. Childhood growth was assessed using weight-for-age Z-scores (WAZ), height-for-age Z-scores (HAZ) and body mass index (BMI)-for-age Z-scores (BAZ). Data collection further included socio-demographic data, HIV disease severity, tuberculosis (TB) co-infection, CD4 counts/percentages and HIV viral loads. All children received routine vitamin supplementation, along with nutritional supplementation if malnourished.

Results: The 159 children had a median age of 1.9 years [interquartile range 1.1; 3] and male:female ratio of 1.24:1. In 65.8% of cases the mother was the primary caregiver, 71.4% were staying in brick houses, 83.2% had electricity and 81.5% a fridge. Majority of children presented with advanced or severe clinical disease (n=145; 90.2%) and immunosuppression (n=144; 89.3%), and tuberculosis (TB) co-infection occurred commonly (n=68; 42.8%). Malnutrition at ART initiation was prominent, with a mean WAZ of -2.21 (standard deviation (SD) 1.77) and 49.7% being underweight (WAZ<−2). Stunting (HAZ<−2) occurred in 72.9% (mean HAZ -2.91, SD 1.58) and 18.8% were wasted (BAZ<−2) (mean BAZ -0.46, SD 1.78). Younger age (p=0.011) and TB (p=0.003) were associated with being underweight at baseline, while for severe underweight (WAZ<−3) anaemia (p=0.006) and electricity (p=0.002) were additional factors. Underweight after 5 years of ART was associated with baseline TB (p=0.034), electricity (p=0.028), fridges (p=0.027) and baseline anthropometry (WAZ p=0.000; HAZ p=0.000; BAZ p=0.046), while failure to normalize weight in those with baseline underweight was additionally associated with older age (p=0.03), baseline CD4% (p=0.038) and smaller increase in WAZ (p=0.000), HAZ (p=0.012) and BAZ (p=0.001). There was no association with virological suppression (p=0.79) or immune reconstitution (p=1.0). The weight catch-up occurred exclusively during the first 12 months of ART and on regression modelling was significantly associated with baseline TB (p=0.01) and electricity (p=0.043) and with significant interactions between age and ART duration (age group 1-3yrs p=0.032; p=0.000 for >3yrs).

Baseline stunting was associated with male sex (p=0.037) and TB (p=0.002), whereas younger age (p=0.042) was additionally predictive for severe stunting (HAZ<−3). Persistence of stunting after 5 years was associated with male sex (p=0.035), electricity (p=0.028), fridges (p=0.027) and baseline anthropometry (WAZ p=0.000; HAZ p=0.000). There was no association with virological suppression (p=0.18) or immune reconstitution (p=0.58). HAZ catch-up occurred over the entire period and on regression modelling was associated with baseline TB (p=0.022) and ART duration (p=0.000).

Conclusions: Baseline malnutrition was a major clinical concern in this cohort of HIV-infected children. Weight catch-up occurred in the first 12 months of treatment, while height catch-up happened over the entire 5-year period. Early HIV-identification and ART initiation, childhood TB prevention and poverty alleviation are crucial to ensure optimal growth in HIV-infected children.

No conflict of interest

Abstract: 117

Comprehensive Pediatric HIV care

HIV-Infected Adolescent and Caregiver Experiences of HIV Stigma and Discrimination in Kenya

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Background: There are few data exploring how HIV stigma affects the lives and HIV care of
those infected or affected by HIV. We sought to better understand how HIV stigma is experienced by HIV-infected adolescents and caregivers in Kenya.

**Materials & Methods:** We conducted a qualitative study using focus group discussions (FGD) at 3 HIV clinics in western Kenya. Separate FGDs were held for HIV-infected adolescents (aged 10-14 years) and for caregivers of HIV-infected children. A trained facilitator led FGD in Kiswahili using a semi-structured interview guide based in grounded theory and covering multiple aspects of HIV-related stigma. FGD recordings were translated into English, transcribed, and analyzed using constant comparison, progressive coding, and triangulation to arrive at a contextualized understanding of adolescent and caregiver experiences of HIV stigma.

**Results:** Forty adolescents (mean age: 13 years) participated in 5 FGD and 53 caregivers (mean age: 40 years) participated in 6 FGD. Most caregivers were the biological mother of an HIV-infected child (51%), aunt or uncle (19%) or biological father (13%). Participants described 4 types of HIV stigma: perceived, internalized, enacted, and courtesy. Perceived stigma was the most common type of stigma identified by both adolescents and caregivers and was described as a deep fear of discrimination, specifically in the form of facing isolation and gossip within the community. Fears of loss of social support or damage to relationships were more common than fears of physical forms of stigma (e.g., fear of losing jobs, bullying/abuse, or losing community resources.) Fear of stigma motivated a number of treatment-related behaviors including secrecy about HIV status, not taking medicines in front of others, and hiding medicines, although caregivers alone reported attending distant clinics to avoid recognition. Reports of instances of enacted stigma were rarer than these prominent fears would suggest, and were less common with adolescents than with caregivers.

**Conclusions:** HIV-infected adolescents and caregivers described an environment characterized by fear of HIV stigma and discrimination in western Kenya. These perspectives offer valuable insight into the experiences of living with HIV in this setting and may inform interventions.

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**Abstract: 118**

**Coinfections in Hiv infected children**

**Assessing tuberculosis infection prevention measures and barriers to care for health care workers in public health facilities in Malawi**

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**Background:** Nosocomial transmission of tuberculosis (TB) is an important source of infection for both HIV-positive patients and health care workers (HCWs). In Malawi, guidelines exist for infection prevention and control (IPC) but little is known about their implementation. Our primary objective in this study is to assess the implementation and knowledge of IPC measures aimed at reducing nosocomial transmission of TB in health facilities in Malawi. Our secondary objective is to characterize HCWs utilization of TB/HIV services.

**Materials & Methods:** In cooperation with the Malawi National TB Control Programme, we conducted a cross-sectional assessment of IPC measures at seven health facilities supported by the Baylor Tingathe community outreach program in Malawi from September 2014 through January 2015. Three approaches were used: structured interviews with facility managers; completion of an anonymous questionnaire by HCWs; and direct observations of pre-selected IPC measures by researchers.

**Results:** Fifteen manager interviews, 211 HCW questionnaires, and 5 direct observations were analyzed. Notable findings regarding facility implementation of IPC measures included: 47% (7/15) of managers reported active screening for TB amongst patients receiving
Abstract: 119

Implementation research on PMTCT and pediatric treatment programs

Completeness and accuracy of data in Zimbabwe’s national PMTCT program health facility registers: Findings from a patient level data quality audit

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Background: Prevention of mother-to-child transmission of HIV (PMTCT) remains a priority in Zimbabwe. The longitudinal nature of clinical care and multiple entry points for PMTCT services create unique data quality challenges. To ensure quality of program data, it is crucial to conduct data quality audits (DQA) at client and health facility documentation and aggregation levels. Complete and accurate data are required to reliably monitor program achievements and targets. In 2014, the Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) conducted a patient level data quality audit (DQA) of the national PMTCT program to measure completeness and accuracy of data in facility registers, which are used to measure PMTCT program performance.

Material & Methods: A descriptive cross-sectional study was conducted in 43 randomly selected health facilities. Patient level data for pregnant and lactating women and infants aged six weeks to six months were abstracted from patient-held medical cards and facility registers. In addition, exit interview findings with antenatal (ANC) and postnatal (PNC) women were compared with data on patient held cards. Completeness and accuracy was assessed for data elements such as ANC number, age, parity, date HIV tested, HIV test result, date initiated on ART and date of 6 week postnatal visit. A data element was complete if patient held card and facility register were documented, and accurate if documentation on the two sources were the same. Reasons for discordance were explored through interviews with healthcare workers (HCWs). Data were analyzed using STATA 12 and the study was approved by Medical Research Council of Zimbabwe.

Results: Records for 292 ANC and 266 PNC women and their children were reviewed. Overall completeness for ANC data elements was 83% and 71% for PNC; overall accuracy was 75% for ANC data elements and 66% for PNC. Completeness and accuracy of ANC data elements for lower level facilities (clinics and rural hospitals) were higher than referral facilities (mission, district and provincial hospitals). More than 50% of inaccuracy for most data elements including age, gravida, visit date, child date of birth, birth weight and date of 6 week visit was a result of health workers documenting on patient held cards only and not updating facility registers; largely due to health workers prioritizing provision of clinical care in the context of multiple registers and high...
workload. Accuracy based on data from patients’ interviews and patients held cards was above 90% for all assessed data elements.

**Conclusions:** The variation in completeness and accuracy by facility type calls for targeted on-site mentoring and coaching of facility level health workers. Health worker documentation in patient held cards without updating facility registers was the major determinant of incompleteness and inaccuracy. Dual documentation of services on patient held cards and health facility registers is a challenge for healthcare workers in the context of multiple client registers, staff shortages and larger patient-HCW ratios. There is need to ensure that health workers document in facility registers in order to accurately measure PMTCT service uptake.

*No conflict of interest*

**Abstract: 120**

**Coinfections in HIV infected children**

**Prevalence of proteinuria in HIV infected Indian Children**

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**Introduction:** HIV infection is increasingly becoming an important cause of childhood morbidity and mortality in India. There are a variety of renal disorders that complicate HIV infection including the distinctive lesion of HIV associated nephropathy. There is a paucity of studies on prevalence of HIVAN in India. The objective is to study the prevalence of proteinuria in unselected HIV infected children aged 18 months to 18 years attending paediatric ART clinic.

**Methods:** In this cross sectional study 139 HIV infected children between age group 18 months and 18 years were recruited from the ART centre of a tertiary care hospital in New Delhi, India. Persistent proteinuria was diagnosed by urinary dipstick finding of 1+ or more on two or more occasions in the absence of fever and a urine protein-to-creatinine ratio (each measured in mg/dl) of ≥ 0.2. Urine protein and urine creatinine were measured by colorimetric and an enzymatic method respectively. If the above mentioned criteria was negative then urinary albumin to creatinine ratio was measured to detect microalbuminuria (ACR = 30 – 300 mg/g) by collecting urine sample in the subsequent visit. Urinary albumin was measured by using immune-turbidimetric method.

**Results:** The prevalence of proteinuria in this study was 11.5%. Prevalence of microalbuminuria was 10.6% in normoproteinuric group and 9.35 % in the total study population. The prevalence of albuminuria (urinary ACR ≥ 30 mg/g) was 20.9% among HIV positive cases. The prevalence of proteinuria increased with WHO staging, 8.05% in stage 1 to 26.32% in stage 3+4 (Table1). No statistically significant relation of proteinuria or microalbuminuria was found with duration of HAART and CD4 count.

**Conclusion:** Screening for proteinuria and microalbuminuria can help in early detection of renal disease in HIV positive patients, which may help in decreasing the progression of to ESRD by early institution of appropriate therapy.

*No conflict of interest*

**Abstract: 121**

**Comprehensive Pediatric HIV care**

**Yield of Provider-initiated testing and counselling among hospitalized children at public Hospitals in Northern Ethiopia**

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Abstract

Introduction: Provider-initiated testing and counselling (PITC) at different child health service entry points, is a common approach to identify new HIV-exposed and infected children. WHO recommends performing PITC for children attending health facilities seeking medical services. Although PITC is not practiced uniformly in all facilities, the Ethiopian national guideline implemented at the end of 2008 also endorses routinely offered HIV testing for all hospitalized children. The aim of this study is to assess the practice and determine the yield of PITC among hospitalized children aged 0-14 years in public hospitals located in Northern Ethiopia.

Materials & Methods: We conducted retrospective reviews of the PITC registers from May, 2009, to April, 2011, used on the admission wards at three public hospitals, located in Bahirdar in Amhara and Mekele in Tigray. The hospitals were selected given their location in cities with reported high urban adult HIV prevalence as of 2009 (Bahirdar [9.8%] and Mekele [10.8%]). Felege Hiwot referral hospital (FHRH), in Bahirdar, and Mekele & Ayder referral hospitals in Mekele city were included in the study. Structured forms were used to collect relevant data including HIV testing status, HIV test results and admission diagnosis from PITC registers. Data entry and analyses was done using Microsoft Office Excel 2010.

Results: A total of 2,081 children were tested in the three hospitals in the first year of the study period, and 137 HIV positive children were identified. In the second year, the number of children tested and identified HIV positive increased by 21.6% and 6% respectively. Over the study period, of 2,611 children with unknown HIV status offered testing at FHRH in Bahirdar city, 2,398 (92%) children were tested and, 168 (7%) were HIV positive. Among children tested at FHRH, 1,700 (68%) were aged less than five years. In Mekele, at the two referral hospitals, 2,212 (91%) of the total 2,442 offered children with unknown HIV status, were tested for HIV, of whom 114 (5%) were positive. Among children tested at the two hospitals in Mekele, 1,409 (64%), were aged less than five years. In Bahirdar, at FHRH, pneumonia (40%) and malnutrition (16%) were the leading primary admission diagnoses among children with HIV positive results. Likewise, malnutrition (35%) followed by pneumonia (21%) accounted for the majority of primary admission diagnoses among HIV positive children admitted at the two hospitals in Mekele.

Conclusions: Implementation of routine HIV testing for hospitalized children resulted in growing number of children tested and diagnosed for HIV in the three facilities. PITC in these hospitalized children yielded an average of 6% HIV positivity. PITC at pediatric inpatient settings provides opportunities for identification and linkage of HIV positive children to care and treatment services.

No conflict of interest

Abstract: 122

Coinfections in HIV infected children

Outcomes in HIV-infected children with clinically diagnosed tuberculosis in Kenya

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Introduction: Diagnosis of tuberculosis in HIV-infected children continues to rely on clinical algorithms in many resource-limited settings. We describe outcomes and diagnostic probability in applying recently published proposed case definitions to a historical cohort of HIV-infected children clinically diagnosed with TB at three sites in Kenya.
Materials & Methods: Between March 2009-December 2010, 689 HIV-infected children aged 6 weeks to 14 years were screened for tuberculosis. Diagnosis was made according to Kenya National Guidelines using chest x-ray, tuberculin skin test, and TB score chart. Symptoms and clinical response were retrospectively evaluated at baseline, 2 and 6 months after initiation of TB treatment. Clinical response was defined as weight gain and absence of TB-related symptoms. Symptom prevalence at each time point was compared using population average (generalized estimating equation) models, including log-binomial models for relative risk of cough and fever and linear models for weight-for-age Z-score and the natural log of CD4+ count.

Results: Of 689 children screened, 59 (8.6%) TB cases were identified with a median age of 5.4 years (IQR 3.11, 8.17) of which 34 (58%) were on HAART. Cough declined significantly from baseline to both 2 months (RR 0.25; 95%CI 0.14, 0.46) and 6 months (RR 0.43; 95%CI 0.28, 0.67) as did fever at 2 months (RR 0.09; 95%CI 0.02, 0.33), and six months (RR 0.13; 95%CI 0.04, 0.37). Weight-for-age Z-scores increased by 0.26 by 2 months and 0.53 from baseline to 6 months. CD4+ counts did not show a significant response. Overall, 29 (49%) and 35 (59%) children demonstrated a good clinical response at 2 and 6 months after initiating treatment. Including clinical response as part of case definition, 39 cases (66%) were classified as probable, 14 (24%) possible, and 6 (10%) uncertain.

Conclusions: The majority of HIV-infected children clinically diagnosed with TB demonstrate improvement following initiation of anti-TB treatment. A significant proportion continues to have symptoms possibly related to misdiagnosis, immune reconstitution inflammatory syndrome, or time on HAART.

No conflict of interest
the outcomes achieved with the different strategies.

**Results:** Program outcomes - Number of PMTCT sites increased rapidly with DBA compared to FCA (from 50 to 814). There was increase in number of pregnant women tested for HIV per year (from 30,000 to 140,000). Number of WLHIV enrolled in the program per year remained same (200). The proportion referral cases to the sites was 77% and 79% with FCA and DBA respectively. Increased uptakes of CD4 testing (87 vs. 96%), mother ARV (83 vs. 92%), baby ARV (91 vs. 98%), baby HIV testing (78% vs. 87%); were seen with DBA compared to FCA. 72% infected women and all infected infants were linked to free ART services with DBA.

**Challenges and opportunities** - The DBA ensured good quality PMTCT counseling and care especially to HIV infected women. It enables rapid scale up in private sector and strengthened linkages between private-public sectors. However, sustaining quality of comprehensive antenatal counseling and pre-test HIV counseling was challenging, raising the possibility of violation of rights of the woman for informed HIV testing. Despite rapid increase in sites, annual number of WLHIV reached through the program remained the same. This could be due to declining HIV prevalence as well as large number of HIV positive referrals. The cost sharing model (PPP) in DBA increased sustainability of the project.

**Conclusions:** The district based approach helps in rapid saturation of PMTCT services in private sector, establishes strong referral systems and partnerships within the program. As the programs adopt this approach, additional efforts would be needed to improve comprehensive antenatal care services.

*No conflict of interest*

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**Abstract: 124**

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

**Are women enrolled in the PMTCT program breastfeeding their infants? - Findings from a PMTCT electronic database in Zimbabwe**

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**Background:** Breastfeeding remains the optimal method of feeding for all newborn infants. In addition, socio-economic factors make breast-feeding an important source of nutrition for infants 6 months and under in the developing world. The WHO introduced new infant feeding guidelines for HIV-infected women in 2010 in the background of global evidence demonstrating poor survival amongst HIV-exposed, non-breastfed infants. Knowing that the majority of women in the country would not have the resources to safely formula feed, Zimbabwe adopted the WHO 2010 Option A guidelines in 2011; with a recommendation for a 2 year breastfeeding period with use of antiretroviral prophylaxis. In 2013, Zimbabwe further adopted the WHO 2013 Option B+ guidelines and maintained the policy on breastfeeding, recommending exclusive breastfeeding for the first 6 months of life, with introduction of solids and continued breastfeeding up to 24 months. However, challenges still exist in monitoring breastfeeding patterns amongst HIV infected mothers attending health facilities in Zimbabwe and in assessing final post-breastfeeding HIV status for HIV exposed babies.

**Materials & Methods:** As a key partner to the Zimbabwe PMTCT program, in 2011, the Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) developed an electronic database (EDB) that captures data from facility registers for all women attending antenatal and postnatal care. This database is active at 36 representative MNCH sites throughout Zimbabwe.
Zimbabwe. Data collected includes but is not limited to monthly breastfeeding trends from birth to 24 months as well as post breastfeeding HIV testing. Results are used for program monitoring and to make recommendations to improve program performance.

**Results:** Completeness of breastfeeding data captured in the registers covered by the EDB varies from considerably from site to site. Indicators are also not designed to adequately capture breastfeeding trends. Confirmatory 18 month and post breastfeeding rapid tests are only done in about 10% of cases; and consequently post breastfeeding maternal to child HIV transmission (MTCT) rates cannot be routinely analyzed. However, from January to December 2013, 6 week exclusive breastfeeding amongst HIV infected women at these sites remained high at 94%. At three months pot partum, 73% are still exclusively breastfeeding; although this proportion falls to about 21% at the sixth month review.

**Conclusions:** The change in guidelines that allow HIV infected women to breastfeed with use of ART prophylaxis have been well received; particularly in poorly resourced countries such as Zimbabwe, where the majority of women are unable to safely use replacement feeding. However, guidelines on 6 month exclusive breastfeeding are only being adhered to by a fifth of women attending EDB sites in Zimbabwe. In addition, without adequate data that allows monitoring of breastfeeding MTCT rates, it will be challenging to monitor the effectiveness of the PMTCT program in the country. There is therefore an urgent need to strengthen infant feeding counseling for HIV infected mothers, mentor and support healthcare workers to conduct final HIV determination tests on HIV exposed breastfed infant and strengthen the quality and rate of completeness data in health facility registers. EGPAF is currently supporting the Ministry of Health and Child Care in these critical areas.

**No conflict of interest**

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**Abstract: 125**

**Comprehensive Pediatric HIV care**

**HIV encephalopathy and bilateral lower limb spasticity despite early antiretroviral therapy in South African children**

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**Background:** Diagnosis of HIV encephalopathy in children includes the presence of acquired motor deficits such as bilateral lower limb spasticity. Nevertheless, much remains to be learned about the natural history of bilateral lower limb spasticity when associated with HIV and what factors influence the functional status of children with this condition. Therefore, the aim of the current study was to investigate possible relationships between the functional status of children with bilateral lower limb spasticity as part of an HIV diagnosis and i) age at starting anti-retroviral treatment (ART) and ii) chronological age.

**Materials & Methods:** Children with perinatal HIV infection and bilateral lower limb spasticity as part of a confirmed HIVE diagnosis were recruited from around Cape Town, South Africa, for this cross-sectional study. Clinical data was obtained from medical records and Gross Motor Function Classification System (GMFCS) levels were assigned. Functional status was measured using the Gross Motor Function Measure (GMFM-88), which assesses performance of 88 items grouped according to 5 types of activity. Percentage scores were calculated for each activity domain and as a total score with 100% indicating that all items were successfully completed. GMFCS levels were compared using a Kruskal Wallis test and Dunn’s post-hoc test and associations between age and GMFM outcomes were investigated using Spearman’s correlations. Significance was accepted at $p < 0.05$. 

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Results: Twenty-six children were included in the study (11 boys, 15 girls, mean age ± SD 8y5mo ± 2y1mo, range 5y1mo-12y10mo)(GMFCS I, n=9 ; GMFCS II, n=11 ; GMFCS III, n=6). Mean age at the start of ART was 7 ± 3mo, range 3-13mo. Children obtained a mean score of 86.4 ± 11.0 % (range 61.7-99.2 %) for the total GMFM-88 assessment and 66.4 ± 27.5 % (8.3-98.6 %) for the GMFM-88 'Walking, Running and Jumping' domain (GMFM E). There was no significant difference in age at the start of ART or current age between the GMFCS level I, II and III groups. Furthermore, there were no significant correlations between age at the start of ART and GMFM-88 or GMFM E score and no significant correlations between current age at GMFM-88 or GMFM E score (r = -0.13 to -0.26, p >0.05).

Conclusions: Despite commencing ART within 3-13 months, all children in the current study had bilateral lower limb spasticity as part of an HIVe diagnosis and showed varying levels of functional impairment. Functional status was not significantly related to age at ART initiation or to chronological age. These observations suggest that even earlier ART initiation may be necessary to prevent HIVe. However, it is also likely that there are other factors that increase a child’s risk of developing HIVe despite ‘early’ ART initiation. Future studies could investigate genetically-based risk of HIVe, HIV disease progression at the start of ART and history of viral load suppression as factors which might influence the functional status of children with HIVe, providing further insight into the aetiology and optimal management of this condition.

No conflict of interest
adolescents noted their caregivers expected more negative reactions.

**Conclusion:** Adolescents in western Kenya provided valuable insights (e.g. considering maturity level before disclosure and disclosing gradually over time) into preferred practices of disclosure timing and methods. Clinicians should explore how children's beliefs, preferences, and needs can be incorporated into disclosure.

No conflict of interest

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**Abstract: 127**

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

**Growth of Southern African HIV-exposed uninfected infants in the first 6 months of life**

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**Introduction:** HIV-exposed uninfected infants (HEUI) are a growing population in southern Africa especially with increasing coverage of more effective prevention of mother-to-child transmission (PMTCT) antiretroviral (ARV) regimens. We examined factors impacting birth weight and assessed growth within the first 28 weeks of life in South African HEUI.

**Materials & Methods:** This is a retrospective cohort based on routine clinical data provided to the International Epidemiologic Databases to Evaluate AIDS, Southern Africa (IeDEA-SA) collaboration. Two cohorts were included representing the years 2007-2013. HEUI were included if they had birth weight recorded and at least one additional weight within the first 28 weeks after birth, with recorded maternal information. HIV-infected infants were excluded. We assessed factors affecting birth weight-for-age z-scores (WAZ) and growth (longitudinal WAZ) using linear regression and mixed effects models respectively.

**Results:** The median birth WAZ of 2621 HEUI (51% male) was -0.65 (IQR -1.46; 0.0). The feeding modalities practised were: 0.5% exclusive breastfeeding, 7.9% unknown breastfeeding, 0.08% mixed breastfeeding and 89.2% formula feeding. Mothers with a CD4 <200 cells/µl delivered infants with a lower birth WAZ (adjusted ß -0.253 [95% CI -0.043; -0.072], p = 0.006) compared to mothers with a CD4 ≥500 cells/µl. Similarly, mothers who did not receive ARVs delivered infants with a lower birth WAZ (adjusted ß -0.39 [95% CI -0.67; -0.11], p = 0.007) compared to mothers who received antenatal ARVs. Antenatal maternal ARVs and CD4 cell count did not affect postnatal growth. Breastfed infants experienced slower longitudinal growth compared to formula fed infants (adjusted ß -0.012 [95% CI -0.021; -0.003], p =0.011). Infants with birth weight <2 500g experienced faster growth within the first 28 weeks of life (adjusted ß 0.070 [95% CI 0.061; 0.078], p <0.0001) compared to infants weighing ≥2 500g.

**Conclusion:** Less severe maternal disease and use of ARVs positively impacts birth weight in this cohort of South African HEUI. Formula feeding was common with breastfed infants experiencing marginally slower longitudinal growth. However, as so few infants were breastfed it is difficult to draw conclusions from this data. Further studies are needed to assess HEUI outcomes in the context of lifelong maternal triple therapy for all pregnant and breastfeeding women.

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Conflict of interest: Funding: National Institute of Allergy and Infectious Diseases and the Eunice Kennedy Shriver National Institute of Child Health and Human Development
Abstract: 128

Prevention of Mother-to-Child transmission

Could Cameroon reach WHO "virtual elimination" of new paediatric HIV infection by the end of 2015? A computer simulation-based assessment

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Background: Cameroon is one of the 21 priority countries in the Global Plan towards the elimination of new paediatric HIV infections by the end of 2015. The country has focused on the strengthening of Preventing Mother-To-Child-Transmission (PMTCT) program services and care of paediatric HIV infections. However, even where effective interventions are available, many women and infants are lost at different steps of the PMTCT cascade, and the extent of MTCT of HIV remains difficult to measure in this context while this is needed for policy makers. We developed a stochastic simulation model to estimate the number of newly HIV-infected children and the MTCT risk (perinatal and postnatal risks) based on the level of the observed and estimated uptake of PMTCT program services at different steps of the PMTCT cascade in Cameroon between 2011-2015.

Materials & Methods: We used a discrete events computer simulation-based approach with a stochastic structure to generate a cohort of pregnant women followed-up in several states during pregnancy until delivery (perinatal transmission), and optionally until complete breastfeeding cessation (postnatal transmission). The different parameters of the simulation model were derived using natural growth models based on results obtained from different data sources in Cameroon: the National AIDS Control Committee, demographic health surveys, field studies and literature.

Results: Available data show a low level of uptake of PMTCT services (antenatal, prenatal HIV testing, PMTCT interventions) in Cameroon between 2011 and 2013. Assuming that the level of uptake of PMTCT services will grow at the same speed over the 2014-2015 period, the overall MTCT rate from birth to 24-months postpartum was estimated at 22.1% (95% CI, [18.6-25.2]) in 2011, 20.1% (95% CI, [17.0-23.2]) in 2012, 19.0% (95% CI, [15.7-21.7]) in 2013, 17.2% (95% CI, [14.3-20.3]) in 2014 and 15.0% (95% CI, [12.0-18.4]) in 2015. The overall MTCT rate take into account the MTCT from prevalent mothers, who acquire HIV infection before delivery, and incident mothers, who acquire HIV infection during breastfeeding. For HIV prevalent mothers, MTCT rate from pregnancy to 24-months postpartum was estimated at 22.8% (95% CI, [18.7-26.6]) in 2011, 21.1% (95% CI, [17.2-25.7]) in 2012, 18.9% (95% CI, [15.6-23.9]) in 2013, 16.5% (95% CI, [13.3-20.5]) in 2014 and 13.3% (95% CI, [9.7-17.1]) in 2015. For incident mothers, MTCT rate from birth to 24-months postpartum was estimated around 19% between 2011-2015. When simulating several PMTCT service coverage scenarios for 2015, the MTCT rate for prevalent mothers was estimated at 3.6% (95% CI, [1.7-5.5]) if access to antenatal care and HIV testing coverage reach 100% and all other PMTCT services reach at least 80%.

Conclusion: Despite substantial efforts increasing access and uptake of PMTCT programme services, the estimated MTCT rate in Cameroon remains high. To reach the goal of 'virtual elimination' of paediatric HIV by the end of the year, the national strategic plan needs to increase the coverage of access to antenatal care and HIV testing to 100% for HIV-infected prevalent pregnant women. Further analyses are ongoing in order to estimate the extent of HIV infection in lactating women and the consequence on MTCT.

No conflict of interest
Abstract: 129

HIV infection and adolescents

Barriers to adherence amongst adolescents living with HIV in Rwanda

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Background: Poor adherence is driving poor outcomes for adolescents living with HIV. We undertook a study, combining quantitative and qualitative methods, to identify predictors of poor outcomes and barriers to adherence for adolescents enrolled in a new adolescent-friendly HIV service in Rwanda.

Materials & Methods: Adolescents 15-19 years enrolled for at least one year in the adolescent HIV clinics at Centre Hospitalier Universitaire de Kigali and Ruhengeri District Hospital were included. A retrospective case note review of demographic and clinical data from 2013 - 2014 was conducted. Included adolescents were then interviewed on their treatment adherence using the Visual-Analog-Scale (VAS), HIV-related knowledge, barriers to care, satisfaction with care services, and psychological state using Beck-Depression-Inventory (BDI).

Results: 199 adolescents were enrolled. The median-age of enrollment was 16 years and 89% (177 of 199) had initiated ART. 27% (47 of 175) had immunological failure (>50% decrease from peak CD4 or CD4 decrease to below pretreatment value). 51.3% (73 of 142) had complete viral suppression (viral-load of <40copies) and 37% had viral-load failure (>1000copies). 55.6% (79 of 142) reported adherence of 85% or less on VAS. 49% (96 of 197) demonstrated depression. 84.4% (167 of 198) reported that they were satisfied with the adolescent-clinic-services provided.

Self-reported adherence to ART (OR= 2.1; 95%Ct= 1.31-2.89; p <0.05) and not being in boarding school (OR = 1.80; 95% CI = 1.08 – 2.52; p<0.05) were associated with viral suppression. Depression was significantly associated with virological failure (OR=0.92; 95%CI=0.88-0.96; p<0.05).

Conclusions: These findings serve to provide useful lessons that can help strengthen efforts for adolescents living with HIV in Rwanda. To sustain adherence, dedicated HIV services must be tailored to the unique needs of adolescents, including educational, socioeconomic, and psychosocial supports.

No conflict of interest

Abstract: 130

Prevention of Mother-to-Child transmission

Mother-to-child transmission of HIV in Ghana: Assessing the trend and the level of awareness

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Introduction: Mother-to-child transmission of HIV (MTCT) accounts for most of the new HIV infections in children. An HIV-positive pregnant woman is who is not on any preventive intervention has a very high chance of transmitting HIV to her baby during pregnancy, delivery and breastfeeding. Ghana being one of the countries with highest burden of HIV in pregnant women has been carrying out various activities targeted in increasing the MTCT knowledge through several preventive and control programmes over the years. The objective of this study was to assess the trend and progress made by Ghana through awareness measures.

Materials & Methods:

Study data from Ghana Demographic and Health Surveys (GDHS) were used to ascertain the trends in percentage of women age 15-49 and men age15-59 who knows that HIV can be transmitted from mother to child by...
breastfeeding and that risk of MTCT of HIV could be reduced by mother taking special drugs during pregnancy. The 2003 and 2008 GDHS were used for this purpose. Matched-pairs t-test was used to evaluate the trend and level of awareness.

**Results:** A total of 19195 participants took part in the two surveys, with women accounting for 55% participation. In 2003 only 172 (15%) of the female respondents had comprehensive knowledge of PMTCT but this increased to 462 (47%) in 2008, p= 0.00026. For their male counterparts, it was 126 (13%) in 2003 and 312 (38%) in 2008, p= 0.05345. In 2008, the age group 25-29 years had the highest level of awareness among women (53.7%) while 30-39 group had the highest proportion among men (42%). The age group 15-19 years had the least proportion of knowledge among both women and men. More urban men and women had comprehensive knowledge of prevention of mother-to-child transmission of HIV than their rural counterparts.

**Conclusions:** There was an increase in MTCT knowledge over the years, however the increase is very significant among women while it was not significant among men. The rural people are less knowledgeable than the urban dwellers. This shows various awareness programmes in Ghana had impact and has yielded positive results. There is still need to improve and re – strategise on the present awareness measures especially among the age groups that are having lower level of awareness. Attention should also be given to men by developing programmes that are more focused on the men folks in order to achieve higher level of awareness.

*No conflict of interest*

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**Abstract: 131**

*Prevention of Mother-to-Child transmission*

**Pregnancy and Contraception: The Perspective of HIV-Positive and Negative Women**

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**Background:** To understand pregnancy intentions and contraception knowledge and use among HIV-positive and negative women in the prevention of mother-to-child transmission (PMTCT) program in the teaching hospital.

**Materials & Methods:** A cross-sectional survey of 236 HIV-positive and 162 HIV-negative postpartum women interviewed within 18 months of their expected delivery date in a public-sector health facility providing PMTCT services. Bi-variant analyses explored fertility intentions, and family planning knowledge and use by HIV status. Multivariate analysis identified socio-demographic and service delivery-related predictors of reporting a desire for additional children and modern family planning use.

**Results:** HIV-positive women were less likely to report wanting additional children than HIV-negative women (8 vs. 49%, P < 0.001), and although a majority of women reported discussing family planning with a health worker during their last pregnancy (HIV-positive 79% vs. HIV-negative 69%, P = 0.0), modern family planning use remained low in both groups (HIV-positive 43% vs. HIV-negative 12%, P < 0.001). Condoms were the most commonly used method among HIV positive women (31%), whereas withdrawal was most frequently reported among HIV-negative women (19%). In multivariate analysis, HIV-negative women were 16 times more likely to report wanting additional children and nearly 85% less likely to use modern family planning. Women who reported making two or less antenatal care visits were 77% less likely to use modern family planning.

**Conclusion:** Our results highlight success in provision of family planning counseling in PMTCT services. As family planning use was low among HIV-positive and negative women, further efforts are needed to improve uptake of modern methods, including dual protection, in the PMTCT settings.

*No conflict of interest*
Abstract: 132

Prevention of Mother-to-Child transmission

Facilitating community-led action for optimal uptake of Prevention of Mother-To-Child Transmission of HIV (PMTCT) services in vulnerable communities

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Introduction: Zimbabwe’s Demographic Health Survey (ZDHS) 2012 shows 65% of births occur in health facilities. The survey highlights strong relationship between uptake of antenatal care (ANC) and place of delivery. These high levels of home deliveries (35%) threaten Zimbabwe’s efforts to eliminate pediatric AIDS, as opportunities are missed to test women and ensure enrolment in prophylaxes. Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) engaged communities in targeted regions to promote actions that address hindrances associated with suboptimal uptake of PMTCT services.

Materials & Methods: Manicaland Province was targeted for support due to high home delivery rates (35.7% of deliveries occur at home here). This rate is likely due to local beliefs that oppose biomedical interventions. In 2014, EGPAF facilitated community stakeholder dialogues in five districts in the province. Six Dialogues gathered community residents and leaders (religious and political) within a health facility catchment area to discuss PMTCT, build local understanding and promote ownership of the community’s roles in supporting optimal uptake of PMTCT services including institutional delivery. Partnering with other local health organizations, health services such as HIV testing and counseling, CD4 count testing, ANC, and well-baby checks were offered to residents during the dialogues. Aggregate PMTCT cascade data from local health facilities were presented, followed by discussions with different population groups (men, women, community leaders, youths, etc.) on their role to support PMTCT services.

Results: Nearly 4,000 people attended six community dialogues. Community leadership expressed appreciation of the platform to discuss local PMTCT aggregate data and understanding challenges associated with barriers to optimal service access. Local- led actions, based on decisions made during the dialogues included: community leaders in one district committed to building a shelter to provide temporary residence for expectant mothers to avoid the long distances; the local council in the same district allocated land for the shelter and a community business operator committed resources; In another district, the community raised its own resources and organized another community dialogue in a separate ward to address religious objections for facility deliveries.

Conclusions: Community dialogues promoted local-led action to addressing hindrances associated with sub-optimal uptake of PMTCT services.

No conflict of interest
Abstract: 133

HIV infection and adolescents

Adolescent and Caregiver Perspectives on HIV-Related Stigma in Kenya: Insights for Measuring and Reducing Stigma for Families

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Introduction: HIV stigma is a major barrier to HIV prevention and treatment, yet few contextual data inform stigma reduction interventions. We explored adolescent and caregiver perspectives on HIV stigma specifically related to measuring and reducing stigma for families in Kenya.

Materials & Methods: We conducted a qualitative study using focus group discussions (FGD) at 3 HIV clinics in western Kenya. Separate FGDs were held for HIV-infected adolescents and for caregivers of HIV-infected children. A trained facilitator led FGD in Kiswahili (a widely used regional language) using a semi-structured interview guide based in grounded theory and covering multiple aspects of beliefs about HIV stigma. FGD recordings were translated into English, transcribed, and analyzed using constant comparison, axial coding, and triangulation to arrive at a contextualized understanding of adolescent and caregiver perspectives on measuring and reducing stigma.

Results: Forty adolescents (mean age: 13 years) participated in 5 FGD, and 53 caregivers (mean age: 40 years) participated in 6 FGD. Most caregivers were biological mothers of HIV-infected child (51%), aunts or uncles (19%) or biological fathers (13%). For methods of stigma measurement, adolescents and caregivers strongly preferred one-on-one or group counseling versus questionnaires. Participants identified potential indicators of stigma in 3

major areas: physical (e.g., appearing ill or 'dirty'); clinical (e.g., poor adherence); and, psychological (e.g., depression). Caregivers highlighted educational campaigns, particularly those led by healthcare workers in rural areas where stigma is most rampant, as critical to changing attitudes and discriminatory practices. Participants promoted opportunities for interaction between HIV-infected and non-infected community members, including clinics that do not segregate services based on HIV status. Stigma reduction strategies among those infected or affected by HIV centered on increasing family and friend support and services like counseling. Treatment access, adherence and economic security were associated with decreased vulnerability to stigma and connected with the idea that improvement of physical appearance would decrease stigma. Not disclosing HIV status was an important way to avoid potential stigma and discrimination for many participants.

Conclusions: Kenyan adolescents and caregivers provided critical insight for stigma reduction interventions in terms of how stigma may be measured and intervention design in this setting.

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

Lost opportunities to identify HIV-infected patients: a comprehensive study of provider-initiated HIV testing and counseling (PITC) in Malawi

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Introduction: Early diagnosis and treatment of HIV improves patient outcomes and minimizes risk of transmission. Provider-initiated testing and counseling (PITC) is an effective case-finding strategy, but implementation models vary. Malawi Ministry of Health (MOH) guidelines recommend routine opt-out PITC, in line with WHO recommendations for countries with generalized epidemics, but little is known about its implementation. Our objective was to assess PITC implementation in Malawi.

Material & Methods: We conducted a cross-sectional study of PITC implementation at 118 clinics and wards within 12 MOH facilities in central Malawi during June-July 2014. Qualitative data detailing PITC practices was collected through structured interviews with 71 providers who conduct HIV testing at their facility, and characterized using standardized definitions. Routine PITC was defined as the provider offering an HIV test to all patients who have never been tested for HIV test or who received a negative test result more than three months prior. Routine PITC was further subdivided into routine opt-in PITC, when patients must affirmatively agree to the HIV test, and routine opt-out PITC, when patients must specifically decline the HIV test. Symptom-based PITC is a separate category defined as the provider offering an HIV test to patients they suspect are exhibiting symptoms of underlying HIV-infection. Quantitative data describing patient visits and HIV tests recorded during 2013 was abstracted from MOH HIV testing reports.

Results: Variable models of PITC were reported across facilities and departments. Overall, symptom-based PITC was most commonly reported. Only antenatal and maternity (20/24) departments reported implementing routine opt-out testing. Use of a PITC register varied significantly according to department type. Only 7.7% (86,657/1,102,802) of patient visits in 2013 included an HIV test. Subgroup analysis of TB and antenatal clinics with available data demonstrated that HIV status was ascertained in 94.3% (5,293/5,615) and 86.8% (26,831/30,961) of patients, respectively. Providers most commonly cited test kit shortages (71/71 providers), inadequate physical space (58/71), and inadequate number of HIV counselors (32/71) as challenges in PITC implementation. Providers from inpatient units cited the inability to test on weekends (8/16).

Conclusions: Various models of PITC concurrently exist at MOH facilities in Malawi. Only antenatal and maternity clinics demonstrated high rates of routine opt-out PITC. The low ratio of facility visits that included an HIV test suggest missed opportunities for HIV testing. However, the high proportion of patients at TB and antenatal clinics with known HIV status suggest routine testing is feasible. These results underscore the need to develop clear, standardized PITC protocols and tools, and to address obstacles of limited health commodities, infrastructure, and human resources.

No conflict of interest

Abstract: 135

Coinfections in Hiv infected children

The impact of a new diagnostic algorithm on identification of pediatric Mycobacterium TB cases in Mozambique

Reviews in Antiviral Therapy & Infectious Diseases 2015_8
Background: In high burden Tuberculosis (TB) settings, the WHO estimates that 10-20% is pediatric TB. In Mozambique, TB incidence is 544/100,000 persons with only 8% of pediatric TB cases. A clinical diagnostic algorithm was introduced in 2014 to improve the diagnosis of pediatric TB. The algorithm relies solely on the presence of signs/symptoms and TB exposure, without requiring additional diagnostics. In April-June 2014, healthcare workers at ICAP supported health facilities (HF) in Nampula province were trained on the new algorithm. We evaluated the impact of the algorithm on the proportion of pediatric TB cases diagnosed among all new TB cases.

Materials & Methods: Routinely collected aggregate data from the pre-rollout (October 2013-March 2014) and post-roll out (July-December 2014) periods from 32 HF were analyzed. The national TB data does not disaggregate by age all new cases of TB. However, data on HIV testing for all new TB cases are age disaggregated. In both periods at all HF, over 96% (median 100%) of all new TB cases were HIV tested. Therefore data on HIV testing, disaggregated by age, were used as a proxy for age disaggregation of the new TB cases.

The uptake of HIV testing among TB cases, proportion of children with TB who tested HIV positive, and the proportion of pediatric TB cases among all new TB cases were compared across 32 HF using weighted paired t-tests for the 'pre' and 'post' periods.

Results: A total of 2,371 new cases of TB were diagnosed in the pre period and 2,606 cases were diagnosed in the post period. HIV testing among all newly diagnosed TB cases was 99.2% (2,353/2,371) pre and 99.5% (2,593/2,606) post (p=0.26). The proportion of children with HIV among pediatric TB cases was 29.1% (55/189) pre and 33.5% (115/343) post (p=0.46). The proportion of pediatric TB cases among all newly diagnosed TB cases was significantly higher in the post-period: 8.0% (189/2,371) vs 13.2% (343/2,606), p= 0.002.

Conclusions: In Nampula, subsequent to the implementation of the new pediatric TB algorithm, the proportion of pediatric TB cases among all cases significantly increased to 13.2% after 6 months of implementation, approaching the target proportion of 15% of the Ministry of Health. In addition, a high prevalence of pediatric TB/HIV co-infection was noted in both periods.

Additional studies, including other provinces, with longer periods of observation are warranted to confirm these preliminary results on the impact of the new diagnostic algorithm for increasing the detection of pediatric TB.

No conflict of interest
7th International Workshop on HIV Pediatrics

17 – 18 July 2015, Vancouver, Canada

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<td>Effectiveness of conditional cash transfers to increase retention in care and adherence to PMTCT services: A randomized controlled trial</td>
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<td>Zhou, A.</td>
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